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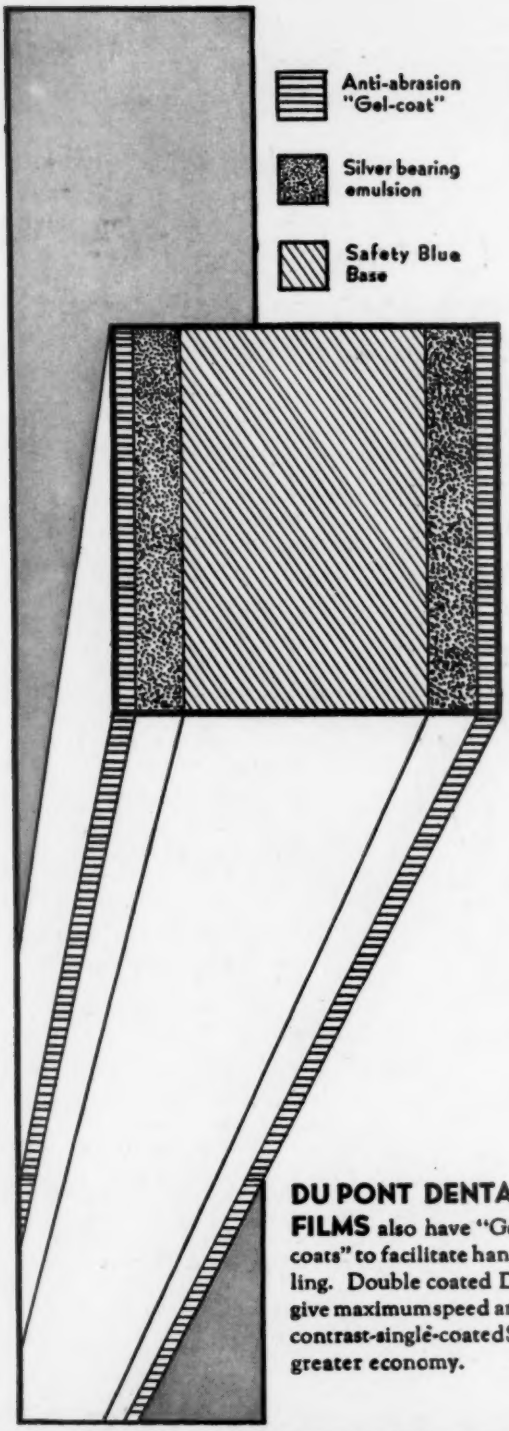

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THE MYELOGRAPHIC DIAGNOSIS OF INTRAMEDULLARY SPINAL CORD TUMORS*

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CHICAGO, ILLINOIS

ALTHOUGH textbooks of neurology frequently state that intramedullary spinal cord tumors may be differentiated from extramedullary tumors by the presence of dissociated anesthesia, practically the differential diagnosis is difficult or impossible.[2,4] If the diagnosis could be established preoperatively, operation which offers only a fair outlook in cases of intramedullary tumor might be deferred or the patient given a more guarded prognosis. Moreover, the knowledge of the type of tumor would allow the surgeon to plan his operation cognizant that the tumor was probably more extensive than the signs and symptoms indicated.

For that reason we have reviewed the series of intramedullary spinal cord tumors seen at the University of Chicago Clinics in the hope of finding myelographic criteria for differentiating intra- and extramedullary neoplasms. In 6 cases of intramedullary spinal cord tumor, verified by operation, lipiodol myelography was used as a diagnostic aid. In 5 of these cases the myelographic findings are similar and, in our opinion, characteristic of intramedullary spinal cord tumor. In the sixth case the roentgenographic picture is not sufficiently typical to permit a definite diagnosis.

REPORT OF CASES

CASE 1. A. H. P., female, aged forty-seven, widow, was referred to the University of Chicago Clinics on May 15, 1939, by Dr. C. Gardner of Aurora, Illinois. During the fall of 1937 she developed an itching and burning sensation in the lower extremities which she attributed to nervousness. She worked hard and under an emotional strain at a job that she disliked. In February, 1938, she fell down a flight of thirteen stairs, landing on the lower part of her back. She was confined to bed for a week. She felt no ill effects except for a little stiffness. In June, 1938, she began to have trouble climbing stairs and was aware of weakness in her lower limbs. On September 7, 1938, she noticed a painless swelling of her left knee. She had great difficulty in walking. About this time she began having sharp shooting pains across her lower back, aggravated by lying down and relieved by sitting. The burning sensation in her legs and difficulty in walking increased.

The past, family and systemic inquiry added no relevant data.

The affective, emotionally unstable attitude of the patient so overshadowed the remainder of her clinical picture that she was suspected of hysteria and admitted to the psychiatric service on May 29, 1939. General physical examination was essentially negative. There was a mild retinal arteriosclerosis. The upper extremities were normal. The lower extremities were somewhat spastic and the patient walked with a peculiar, uncertain, high steppage gait. The Romberg

* From the Division of Neurology and Neurosurgery and the Division of Roentgenology of the University of Chicago. Read before the Chicago Neurological Society, April 18, 1940.

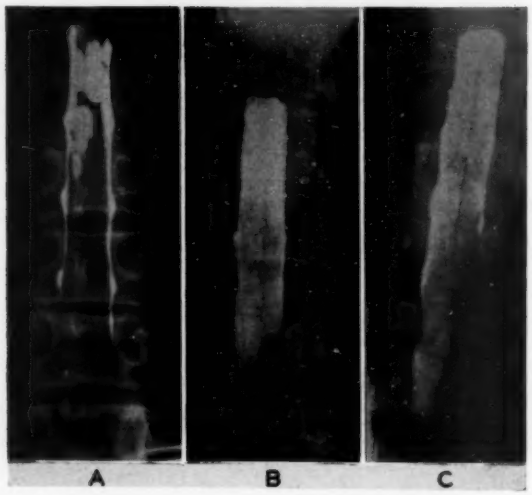

FIG. 1. *A*, Case I. Roentgenogram of the lower thoracic spine taken with the patient in the standing position to show the partial block at the level of the eighth thoracic vertebra and the beaded columns of lipiodol extending down the lateral margins of the spinal canal to the level of the eleventh thoracic vertebra.
B and *C*, Case II. Roentgenograms of the lower thoracic spine taken with the patient on the tilting table head down to show the sleeve-like manner in which the lipiodol surrounded the spinal cord, being finally blocked at the level of the third thoracic vertebra.

test was positive. There was an indefinite sensory loss to pin prick and cotton wool over the lower extremities. Proprioceptive sense was diminished in the feet. Vibratory sensibility was absent in the lower limbs up to the anterior iliac spines. The upper abdominal reflexes were present but the lower ones were absent. The tendon reflexes of the lower extremities were hyperactive. The left patellar jerk was more active than the right and a sustained patellar clonus could be obtained on the left. Both plantar reflexes were flexor in type.

The blood count, urinalysis and Wassermann test on the blood showed no abnormality. Roentgenogram of the spine showed osteoarthritis of the lumbar vertebrae. Free acid was found in the gastric contents after giving histamine.

A lumbar puncture was made between the third and fourth lumbar vertebrae. The initial pressure was 160 mm. of spinal fluid. There was a prompt rise and fall in pressure on jugular compression. Six cubic centimeters of clear colorless fluid were withdrawn and the spinal fluid pressure dropped to zero at the manometer. The spinal fluid contained 30 cells per cu. mm., the majority lymphocytes. The Pandy reaction was +; the total protein 60 mg. per 100 cc. The Wassermann reaction was negative and the Lange curve normal. A week later another lumbar puncture was made. The initial pressure was 120 mm. of spinal fluid. There was no rise in pressure on jugular compression, although abdominal pressure produced a prompt rise followed by a rapid fall. Removal of 6 cc. of clear colorless fluid caused the spinal fluid pressure to drop to zero. Two cubic centimeters of lipiodol were injected. The spinal fluid contained 21 lymphocytes and 7 polymorphonuclear leukocytes per cu. mm. The Pandy reaction was +; the total protein was 50 mg. per 100 cc.

The oil was observed roentgenoscopically with the patient on the tilting table. It passed up to the twelfth thoracic vertebra where it spread out in a peculiar arrangement roughly suggesting the closed petals of a tulip. The following day 1 cc. of lipiodol was injected into the cisterna magna, and the oil observed again on the tilting table. It rolled freely down the spinal canal to the level of the eighth thoracic vertebra where it stopped momentarily and then divided into two columns—one along each side of the spinal canal. These streaks of lipiodol lay close to the pedicles of each vertebra. Between the pedicles of adjacent vertebrae the columns of lipiodol expanded laterally giving the streaks a beaded appearance. The lipiodol was completely blocked at the eleventh thoracic vertebra (Fig. 1, *A*).

After anesthetizing the patient with ether, on June 13, 1939, Dr. P. C. Bucy removed the laminae of the seventh to tenth thoracic vertebrae. The dura pulsated in the uppermost part of the field, but below it was distended and taut. When the dura was opened the spinal cord was found to be pale and greatly enlarged below the eighth thoracic vertebra. Incising the posterior columns the substance of the spinal cord was seen to be spongy and yellowish in color. A thin strip was removed for microscopic study. A bilateral anterolateral chordotomy was done and the wound closed in anatomic layers.

A section taken from the biopsy was found to consist of spinal cord fragments in which the normal architecture was obscured by loosely arranged dentiform cells with many intercellular processes. No mitotic figures were seen. Silver impregnations showed the cells to be astrocytes; therefore a diagnosis of astrocytoma was made.

The postoperative course was slow but satisfactory except that the patient complained of an itching, burning and "terrible" numbness over the lateral aspect of the left leg, although there appeared to be an analgesia below the ninth thoracic segment. The unpleasant paresthesia in her leg greatly diminished. At the time of her discharge June 27, 1939, she was unable to stand or walk, but could move her legs feebly.

Case II. O. R., female, aged thirty-six, stenographer, was referred to the University of Chicago Clinics on January 10, 1940, by Dr. C. L. Leonard of Rockford.

About eleven or twelve years previous to admission the patient began to be wakened at night by stiffness of the neck and pain on movement of the head. During the day the pain was not very noticeable. This nocturnal discomfort persisted until two years before admission when it was replaced by an intermittent pain in her left chest relieved only by lying down. Bending over caused severe pain to shoot down her left arm. The pain occurred in bouts lasting several weeks and recurring every few months. Because of this difficulty she took a prolonged vacation. Upon returning to work in August, 1938, she found that her fingers were too awkward to type. Within a few months she could not even write.

In the spring of 1939 her hands and feet tingled and became numb, making her gait unsteady. The difficulty slowly progressed so that at the time of admission she was able to walk only with the greatest difficulty and with assistance.

Her family history was of significance because one sister died of an intramedullary ependymoma of the spinal cord at the age of thirty-six. One sister and one brother had been institutionalized for mental disease. The patient's past history and functional inquiry added no relevant facts.

Physical examination showed no abnormalities in the thorax or abdomen. On neurological examination no changes were found in the cranial nerves. The thenar and hypothenar eminences were atrophic and the palmar tendons were prominent. The remaining musculature of the upper and that of the lower extremities was generally small and flabby. All four limbs were quite weak and spastic. The tendon reflexes of the left upper extremity were practically absent and those of the right reduced. The abdominal reflexes were absent. Both knee and ankle jerks were exaggerated and the plantar reflexes were bilaterally extensor.

There was a marked, although patchy, hypesthesia to both pin prick and cotton below the third cervical segment without dissociation of these sensibilities. A relative sacral sparing was present. Vibratory sensibility was absent over the lower extremities and in the hands. Proprioceptive sense was almost absent in the hands and feet. Stereognosis was impaired in the hands.

On lumbar puncture the spinal fluid pressure was found to be 65 mm. of spinal fluid. No rise could be obtained on unilateral or bilateral jugular compression although the pressure rose well on abdominal compression. Only 2 to 3 cc. of clear, slightly xanthochromic fluid could be obtained. This gave a slightly positive reaction by Pandy's test. Two cubic centimeters of lipiodol were injected.

Urinalysis and blood examinations showed no abnormalities.

Roentgenograms of the spine revealed a fusion of the laminae of the third and fourth thoracic vertebrae with a narrowing of the interspace. After injection of the lipiodol the patient was tilted under roentgenoscopic control. The oil ran freely up to the eighth thoracic vertebra and then spread out on either side of the spinal cord reaching as high as the sixth thoracic vertebra on the right and the third thoracic vertebra on the left side. Films made with the patient's head down on the tilting table showed that the oil had passed about the spinal cord like a gradually thinning sleeve being finally blocked at the level of the third thoracic vertebra (Fig. 1, *B* and *C*).

After anesthetizing the patient with ether, on January 8, 1940, Dr. P. C. Bucy removed the spines and laminae of the fourth cervical to the second thoracic vertebra. Upon opening the dura a massively dilated yellowish and grayish spinal cord completely filled the canal in the entire field. At one point an aspirating needle encountered 1 cc. of syrupy yellow fluid within the cord substance. The dura was sutured and the muscles closed in anatomical layers.

The patient had an uneventful convalescence except for urinary retention, which was relieved by tidal drainage. She was discharged ten days after operation in much the same condition as at the time of admission except that she was unable to be up and still had difficulty in voiding.

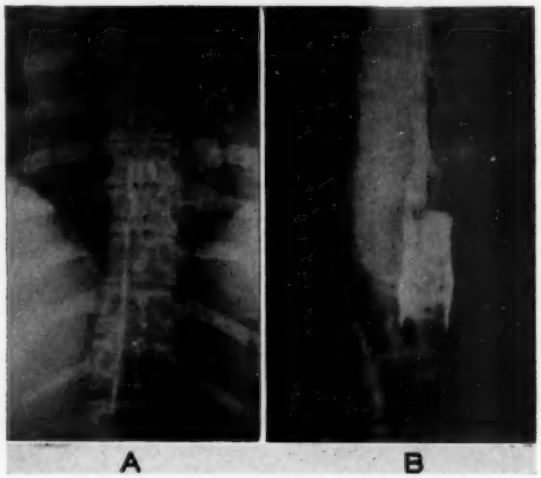

FIG. 2. *A*, Case III. Roentgenogram of the lower thoracic spinal cord with the patient in the horizontal position to show the laterally situated streak of lipiodol and above the tumor the lipiodol lying in a normal position along the middle of the spinal canal.
B, Case VI. Roentgenogram of the midthoracic spine with the patient on the tilting table head down to show the spreading of the columns of lipiodol and the complete block. This picture, although suggestive of intramedullary spinal cord tumor, is not pathognomonic, for other types of tumor may give identical findings.

CASE III. M. H., female, aged forty-two, housewife, was admitted to the University of Chicago Clinics, referred by Dr. O. Balensiefer of LaSalle, Illinois, on December 7, 1937.

The patient had been in good health until April, 1937, at which time her legs suddenly became weak while she was walking and she fell. She was treated by her physician for anemia, with temporary improvement. However, in September, 1937, her legs became so numb and stiff that walking was difficult. She described this sensation by saying that her legs felt "like a ton of bricks." At times the leg muscles quivered and twitched. Her feet were cold and swollen. Ventriculin and liver were given for her anemia. With this therapy the swelling of her legs diminished but the weakness and unsteadiness continued to increase.

In August, 1937, she began to experience difficulty in micturition, finding it necessary to strain several times before she could evacuate the bladder. She had usually been constipated but this condition increased during the summer and fall of 1937 requiring mineral oil every day and stronger cathartics weekly.

Thumping headaches, previously occurring only during her menstrual periods, became more frequent, and were occasionally associated with nausea and vomiting.

During her menses the patient suffered severe backache and on one occasion, following application of an electric pad to her back, found that it was severely burned. She felt no pain from the burn and was entirely unconscious of the injury until the redness of the skin appeared.

Her family, past and functional histories were irrelevant.

Physical examination was essentially negative except for moderate cardiac enlargement and a hypertension of 204/132.

Neurological examination revealed no abnormalities in the cranial nerves and upper extremities. However, the lower extremities were markedly spastic and weak, especially the flexor muscles of the legs. Coordination was poor in the legs and the heel-to-knee test was performed very unsteadily. There was no atrophy, fibrillation or tremor of any muscle in the body.

Sensation was markedly impaired. There was analgesia to pin prick from the sixth to the twelfth dorsal dermatome, and hypalgesia in the lumbar segments. There was almost complete anesthesia to touch with cotton below the ninth dorsal segment. Temperature sensation for both heat and cold was severely impaired below the sixth thoracic dermatome. Vibratory sensibility was impaired below the seventh dorsal segment. Proprioceptive sense in the toes was much diminished.

The tendon reflexes were moderately active and equal in both upper extremities. Knee and ankle jerks were slightly increased on both sides. The plantar reflexes were extensor on both sides.

The patient walked with a stiff, ataxic gait. She could not walk tandem. She showed marked unsteadiness in the Romberg test.

Urinalyses were negative except for a constant trace of albumin. Blood examinations including the Wassermann test were negative.

On December 9, 1937, a lumbar puncture was performed between the third and fourth lumbar spines. The initial pressure was 210 mm. of spinal fluid. With compression on the right jugular the pressure rose to 620 mm., to 400 mm. with compression of the left jugular, and to 700 mm. with pressure on both veins. The rise was quite rapid but the pressure dropped very slowly after release of the jugular compression.

The pressure after removal of 15 cc. of spinal fluid was 90 mm. The fluid was clear and colorless and contained three lymphocytes. Total protein was 56 mg. per 100 cc. The Wassermann reaction was negative and the Lange curve 0011100000.

Roentgenograms of the thoracic spine had shown no abnormality. Because of the history and slight increase in total protein of the spinal fluid, 3 cc. of lipiodol was injected intrathecally by lumbar puncture on December 10, 1937. Following the injection the patient was roentgenoscoped in the head down position and the oil was observed to pass slowly in a thin line along the side of the spinal canal from the second lumbar to the sixth thoracic segment and then drop into the cervical region. This finding suggested a diffuse enlargement of the spinal cord below the sixth thoracic segment (Fig. 2, *A*).

On December 18, 1937, after infiltrating the area with 1 per cent novocaine, the spines and laminae of the sixth, seventh and eighth vertebrae were removed by one of us (A. E. W). Upon opening the dura mater the spinal cord from the sixth thoracic lamina to the inferior margin of the exposure appeared dilated and from the upper margin of the seventh thoracic lamina to about the middle of the eighth thoracic lamina the cord appeared cystic. A longitudinal incision was made in the cyst and extended for a distance of 2 cm. In doing so, a considerable amount of clear fluid was evacuated from the cyst. The inside of the latter was covered with an irregular, trabeculated, grayish-brown, gelatinous substance, which was intimately adherent to the spinal cord substance. The wall did not strip readily so no attempt was made to remove it. Several small pieces were taken for biopsy. The dura mater was placed over the spinal cord without suturing it. After complete hemostasis the muscles were approximated in anatomical layers.

The tumor was composed of loosely arranged cells, some of which were elongated with oval nuclei and a large amount of pale cytoplasm. Other cells were arranged with processes running to blood vessel walls. No mitotic figures were seen. The tumor was a benign glioma, probably best classified as an ependymoma.

The patient had an uneventful but slow convalescence and was given roentgen therapy. She regained sufficient strength in her legs to walk about and do her housework. In March, 1940, following two cerebral vascular accidents, she died at home. An autopsy was not performed.

CASE IV. L. L., female, aged forty-three, housewife, entered the University of Chicago Clinics on May 25, 1939. She had considered herself well until 1927 when she developed urinary frequency which persisted for about three years. Seven years before her admission her legs gradually became weak. This progressed so that seven months before admission she was unable to walk. For three years she had noticed numbness in the lower extremities. This started in the toes and gradually spread upward to involve the legs and thighs. For at least eight months she had been constipated but had considered this due to her inactivity. Six months prior to admission she noticed that her left hand was smaller than formerly. Her voice became weaker and she had a tickling sensation in her throat. About a week prior to admission to the hospital she developed frequent, severe, cramp-like pains in both lower limbs.

From the family history it was learned that a brother of the patient had died at the age of forty from a tumor of the cervical spine. A sister, age unknown, was said to have died of a brain tumor.

The patient appeared emaciated but the general physical examination was essentially negative. The cranial nerves seemed intact, although the reaction of the left pupil to light and accommodation was sluggish as compared to the right. The right vocal cords did not move fully whereas the left moved normally. There was generalized atrophy of the muscles of the trunk and all four extremities, but more marked in the left upper and right lower extremities. The left leg was shorter than the right. There was a marked spastic paraplegia in flexion. All movements of the arms were weak. There was marked limitation of motion in the left hip. Involuntary muscular spasms occurred in both legs. A large blister due to a recent burn from a hot water bottle was present on the lateral surface of the left leg. There was a hypalgesia to pin prick and a marked hypesthesia to cotton wool from the second cervical to the tenth thoracic segment on the right and to the fourth thoracic segment on the left with apparent sparing of the palmar surfaces of the hands. The appreciation of pin prick and cotton was markedly reduced below the second lumbar segment on the right and third lumbar segment on the left side. There was apparent sparing over the posteromedial surface of the left lower extremity and the plantar surface of both feet. Heat and cold could not be differentiated in the areas

of hypalgesia. Vibratory and position sensibility were absent in the lower extremities. The tendon reflexes seemed normally active in the left upper and hyperactive in the right upper extremity. In the lower extremities only a weak patellar response was obtained on the left and no other reflexes could be elicited. The abdominal reflexes were absent.

The patient's temperature was 101.4° F. on admission. The blood showed 4,000,000 red blood corpuscles and 11,200 white blood corpuscles. The Wassermann reaction of the blood was negative. The urine contained 30 pus cells per high power field.

A lumbar puncture was performed on May 26. The initial pressure was 50 mm. of spinal fluid. Bilateral jugular compression brought the pressure to 130 mm.; upon release a slow drop occurred to 100 mm. Abdominal pressure elevated the spinal fluid pressure to 205 mm., followed by a slow drop to 90 mm.; 8 cc. of clear lemon colored fluid was removed. The final pressure was 110 mm. The spinal fluid had 2 cells per cu. mm.; the Wassermann was negative. Protein was +++ by Pandy's test and quantitatively 1,660 mg. per 100 cc. The Lange curve was 5555554333.

Roentgenograms of the spine showed erosion of the right pedicle of the twelfth thoracic vertebra, and incomplete fusion of the spinous processes of the first thoracic vertebra. There was a healed fracture of the neck of the right femur. An air myelography attempted on June 1, 1939, was unsuccessful. The following day another lumbar puncture was made and 1 cc. of lipiodol was injected. Because the iodized oil did not move freely it was considered to be in the epidural or subdural space. This interpretation may be questioned for it is possible that the entire subarachnoid space in the lumbar region was filled with tumor. On June 5, 1939, 2 cc. of lipiodol was injected into the cisterna magna. Under the roentgenoscope the oil was seen to roll down the left side of the cervical canal closely apposed to the pedicles. In places the stream of lipiodol thinned out to a thread. On the opposite side a few drops reached the second cervical vertebra along the pedicle and stopped there. At the level of the first thoracic vertebra, oil again flowed to the right side of the spinal cord. Just below this point it rapidly thinned out and stopped completely at the second thoracic vertebra. This picture suggested an enlargement of the cervical cord, a narrowing at the first thoracic vertebra and a further dilatation just below this point.

On June 6, 1939, after infiltration of the area with 1 per cent novocaine, the laminae from the seventh cervical to the third thoracic vertebra were removed by one of us (A. E. W.). When the dura mater was opened the spinal cord was found to be dilated to about twice its normal size. The enlargement was most marked in the second and third thoracic segments which corresponded to the site of the arrested lipiodol. A bilateral chordotomy was performed. In so doing a cyst lined by a mass of avascular, firm, dark tissue was encountered in the second thoracic segment. A biopsy was taken of the cyst wall. The dura was closed and the wound sutured in anatomical layers.

Microscopically the tumor consisted of loosely packed cells with strands of pink staining, intercellular material. The nuclei of the cells were of many shapes and sizes. There were a few very large cells. No mitoses or areas of necrosis were seen. A pathological diagnosis of astrocytoma of the spinal cord was made.

The postoperative course was satisfactory. The patient was free of all pain in her lower extremities. At discharge on June 10, 1939, the patient's condition was unchanged except for an analgesia below the level of the second thoracic segment.

CASE V. M. D., female, aged twenty-four, single, was referred to the University of Chicago Clinics on September 14, 1936, by Dr. S. P. Morgan of La Porte, Indiana.

For about a year, eight years prior to admission, she suffered nocturnal backaches. Six years before admission, following an appendectomy, she developed a pain in the hips and her legs became so weak that she was unable to walk for three months. She gradually gained enough strength to walk, although her lower extremities remained weak and numb. For four or five years she had been constipated and had some difficulty in starting urination. Occasionally she had fecal incontinence.

The family history was not of medical significance. The general physical examination was negative. The upper extremities were normal. Both legs were weak, especially the flexors of the left knee. Both lower limbs were spastic and ataxic. All modalities of sensation were decreased below the fourth thoracic dermatome. The sensory loss was most marked over the anterior surface of the left lower limb where there was almost complete anesthesia. The tendon reflexes were normally active in the upper extremities, slightly exaggerated in the left lower,

and hyperactive in the right lower extremity. The plantar responses were bilaterally extensor and there was a bilateral ankle clonus.

The blood and urine were normal and the Wassermann reaction of the blood was negative.

On lumbar puncture the initial spinal fluid pressure was zero. With abdominal compression it rose slowly to 200 mm. Bilateral jugular pressure produced a slow rise in 250 mm. followed by a very gradual fall to 150 mm. About 12 cc. of yellowish spinal fluid was removed and 1 cc. of lipiodol was injected. The spinal fluid contained 6 lymphocytes per cu. mm. Globulin as tested by Pandy's reagent was +++ and the total protein was 135 mg. per 100 cc. The Wassermann reaction was negative.

The patient was tilted under the roentgenoscope. The lipiodol flowed along the lumbar canal as a mass to the first lumbar vertebra where it separated into two portions, one of which progressed in a narrow streak along the right pedicles to the first thoracic vertebra and the other along the left side to the twelfth thoracic vertebra. Roentgenograms taken show that the streak on the right side is beaded, presumably due to lipiodol entering the cuffs of the exiting nerve roots (Fig. 3).

After anesthetizing the patient with ether, on September 17, 1936, Dr. P. C. Bucy removed the spines and laminae of the seventh and eighth thoracic vertebra. The exposed dura was moderately tense and did not pulsate. When the dura was opened a dilated spinal cord studded with small cysts was exposed. The spinal cord was incised revealing yellowish, translucent gelatinous tissue with many small cystic spaces. The dura was left open and the wound sutured.

The postoperative course was uneventful. The patient was given roentgen therapy to the thoracic spine. She was discharged October 8, 1936. Her condition was much the same as it had been prior to the operation except for an increase in weakness of the lower extremities. She returned to the Clinics in October, 1939, at which time her condition was unchanged from that at the time of her discharge in 1936.

Case VI. H. H., male, aged fifty-two, farmer, was admitted to the University of Chicago Clinics June 12, 1935, referred by Dr. A. O. Phipps of Manteno.

For three or four years the patient had suffered pain in the back radiating down one or both legs. The aching pain became so severe that he could not sleep lying flat in bed and for two months had to sit up to get relief. The pain then diminished but about eight months before admission he had a sensation of burning and numbness in his feet. His legs became weak and he stayed in bed during part of the winter of 1934–1935. In the spring he felt stronger but required the aid of a cane to walk. He had increasing constipation and at times had precipitate defecation. Micturition was difficult. About six months prior to coming to the hospital he noted a marked loss of libido.

Fig. 3. Case v. Roentgenogram of the thoracic spine showing the thin beaded column of lipiodol lying along the lateral margin of the spinal canal in the entire thoracic region. This is a pathognomonic picture of intramedullary spinal cord tumor.

Family, past and functional inquiries were all irrelevant.

Physical examination showed no abnormalities except those referable to the nervous system. There were no changes in the cranial nerves nor in the upper extremities. Both legs were thin, weak and spastic. The patient was able to walk but only with difficulty and by watching his feet. The tendon reflexes were exaggerated, especially on the left side, and both plantar reflexes were extensor. There was a sus-

tained ankle clonus on the left side. The abdominal and cremasteric reflexes were absent.

There was marked hypesthesia to pin prick, cotton and temperature sensibilities below the sixth thoracic segment, becoming more pronounced below the ninth dermatome. A relative sparing for all modalities was present in the sacral region. Position and vibratory sensibilities were markedly impaired in both legs.

Urinalyses and blood examinations, including the Wassermann test, were negative. A lumbar puncture revealed the spinal fluid to be under a pressure of 125 mm. Upon jugular pressure no rise occurred but when the abdomen was compressed the pressure rose and fell rapidly. Two cubic centimeters of lipiodol were injected intrathecally.

Roentgenograms of the spine showed no evidence of erosion of the pedicles or widening of the spinal canal. Observations of the lipiodol while the patient was being tilted showed that the oil ran freely to the seventh thoracic vertebra. At this level the oil spread apart and for about one segment of the spinal cord appeared as two linear streaks along the pedicles. Then the streak of oil became very thin and stopped (Fig. 2, *B*).

On June 18, 1935, after anesthetizing the patient with ether, Dr. Percival Bailey removed the second to seventh thoracic spines and laminae. Upon opening the dura mater the spinal cord was seen to be markedly dilated, decreasing in diameter at the lower margin of the field. The posterior surface of the cord was incised and a mass of grayish-red tumor, clearly demarcated from the white matter of the cord, was scooped out. No attempt was made to remove all of the tumor. The dura mater was left open and the muscles closed in anatomical layers.

The tumor was composed of pale staining cells, rich in cytoplasm, arranged in layers, and frequently surrounding blood vessels. It was classified as an ependymoma.

The patient had a rather stormy postoperative course, developing a cystitis and pyelitis and decubitus ulcers. He had a complete anesthesia below the fifth thoracic segment and, except for slight movement of the right foot, a complete paraplegia. He was discharged July 4, 1935, and has not been seen again.

DISCUSSION

From these 6 cases the features of myelograms of intramedullary spinal cord tumor may be recognized. It is apparent that the prime characteristic is a partial block with a lateral displacement of the lipiodol so that it lies as a streak or streaks along the pedicles of the vertebrae. The second feature is the presence of a small, lateral, triangular-shaped protrusion from the streak between adjacent pedicles due to the filling of the nerve sheath with lipiodol. To be pathognomonic of an intramedullary spinal cord tumor, the laterally displaced beaded columns of lipiodol must maintain this position for several segments of the spinal cord. Other types of tumor occasionally produce myelograms showing a cap-like obstruction with thinning lateral streaks of lipiodol which, however, do not extend up or down more than one segment. It is for this reason that the myelographic picture of Case VI cannot be considered pathognomonic of intramedullary spinal cord tumor. In 2 cases (I and V) the lipiodol streaked down both sides of the spinal canal apparently outlining the dilated tumorous cord. In the other cases the block was complete on one side so that only one streak of lipiodol is seen.

This differentiation of some intramedullary spinal cord tumors from extramedullary ones is made possible by certain distinguishing biological characteristics of intramedullary growths. Whereas extramedullary tumors usually extend only a short distance along the spinal cord, intramedullary gliomas tend to grow within the cord substance for a considerable distance and in some cases the entire length of the cord. This dilatation of the cord frequently does not occlude the subarachnoid space along the entire extent of the tumor. Since the lateral diameter of the spinal canal is slightly greater than the anteroposterior diameter and the subarachnoid space has small out-pouchings laterally at each nerve root sheath, the portions of the canal that remain patent are the lateral margins. Hence the lipiodol, which usually flows down the anterior wall of the intrathecal space, becomes displaced lat-

erally at the site of the tumor and as the tumor usually extends several segments along the cord before producing a complete block, the lipiodol streaks along the lateral margin of the dilated cord and fills out the nerve sheaths at each segment. The oil may be completely blocked after three or four segments, as in Cases I, II and IV, or it may outline the entire extent of the tumor, as in Cases III and V. It will be apparent that the myelographic picture is pathognomonic only in the case of those intramedullary tumors that extend several segments of the spinal cord before producing a complete block. If a block occurs within one or two segments the myelogram cannot be distinguished from certain extramedullary tumors.

It must be understood that the above myelographic picture is pathognomonic of tumefaction of the spinal cord and not necessarily of neoplasm. Thus a cyst of the spinal cord[5] or a syringomyelia[10] might give the same picture as an intramedullary spinal cord tumor; only by the history and clinical findings could these be differentiated.

It is possible to obtain an approximate idea of the amount of enlargement of the spinal cord by measuring the distance between the lipiodol streaks, but because of the error introduced by the short distance of the tube from the film, these measurements cannot be accepted as the absolute width of the spinal cord.

Knowing this typical picture of intramedullary spinal cord tumor, it is possible to spare a patient an operation which at an early stage in the development of an intramedullary spinal cord tumor would probably be of little benefit. To illustrate this point the following case is presented.

CASE VII. P. Z., male, aged fifty-one, barber, was first seen in the University of Chicago Clinics on December 6 and was admitted to the hospital December 10, 1939. He complained of a dull, aching, almost continuous pain in the abdomen under the right costal margin and sharp shooting pains in one or both shoulders for the past ten years. Seven years prior to admission the patient was told that he had gallbladder and liver disease and should not eat fatty foods. About two years later he noticed that his right leg felt weak and numb and that he walked with a limp. Furthermore, when he was driving his car his right foot would occasionally tremble when placed on the accelerator. At the same time he began to have a dull, aching pain in the back below the shoulder blades and occasional sharp shooting pains in both knees. The pain in the knees could be relieved by walking. For about five years he had some difficulty in starting micturition and for three weeks had dribbling of urine. Two or three years before admission he noticed in the toes of the left foot a feeling of coldness, which spread to involve the entire left leg.

Five weeks before he was seen in the Clinics he took medicine secured from an Indian. Two weeks later his skin became yellow. A local physician gave him four injections and the yellow discoloration of the skin gradually disappeared. He admitted having gonorrhea at the age of forty. His past family and functional inquiry yielded nothing else of medical significance.

The general physical examination was essentially negative. The cranial nerves were normal. The upper extremities appeared normal. There was a slight but definite weakness of the right lower extremity to all movements but no noticeable atrophy. The patient limped on the right foot when walking. There was a hypalgesia to pin prick from the second thoracic to the fifth sacral segments on the left and from the second to the eighth thoracic on the right side. A less marked decrease in appreciation to cotton wool and temperature was present over the areas of hypalgesia. Vibratory sensibility was decreased over the iliac crests. Position sense was normal. Deep pain sensibility was diminished in the left Achilles tendon. The abdominal reflexes were absent. The tendon reflexes of the upper extremities were normally active. Those of the lower extremities were hyperactive, especially on the right side. The plantar reflexes were bilaterally extensor. A sustained ankle clonus was present on the right.

Urinalyses and blood examinations, including the Wassermann reaction, were negative. Roentgen examination of the chest, gallbladder and gastrointestinal tract was negative. Roentgenograms of the spine showed erosion of the right pedicles of the second, third and fourth thoracic vertebrae.

A lumbar puncture showed the initial spinal fluid pressure to be 100 mm. Bilateral jugular compression produced a rapid rise to 220 mm. followed by a slow fall. Abdominal pressure produced a rapid rise to 220 mm. followed by a quick fall. After removal of 5 cc. of clear, colorless spinal fluid the pressure fell to zero. Before the needle was removed 2 cc. of lipiodol was injected. The total protein of the spinal fluid was 416 mg. per 100 cc. The Wassermann reaction was negative.

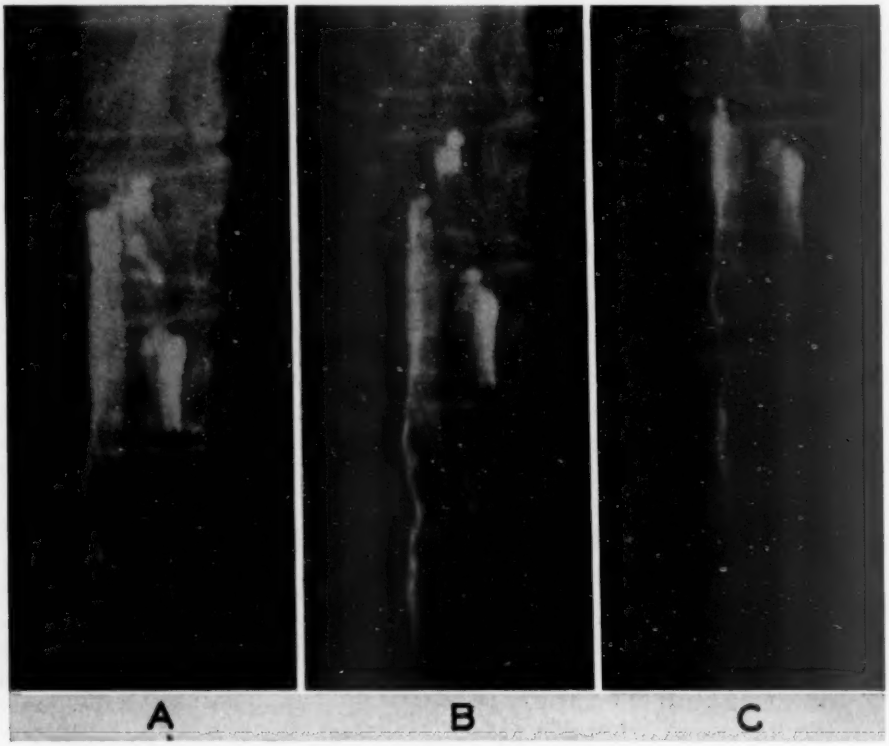

FIG. 4. Case VII. Successive roentgenograms of the midthoracic spine showing the partial block to the lipiodol and the streaking of the lipiodol along the lateral margin of the spinal canal. *A*, roentgenogram taken immediately after assuming the head-down position. *B*, about two minutes later showing the lengthening streak of lipiodol. *C*, three minutes after *B*, showing the still longer streak.

The patient was observed under the roentgenoscope on the tilting table. The lipiodol flowed to the eighth thoracic vertebra where it divided into two lateral columns. The stream on the right side continued as a streak to the level of the third thoracic vertebra and that on the left to the sixth thoracic vertebra (Fig. 4).

This history of this case, the dissociated sensory disturbances and the lipiodol myelography all suggested the diagnosis of intramedullary spinal cord tumor. The patient's good general condition and slight disability made it advisable to defer surgical intervention. Since none of the previous cases were markedly improved by operation, and because even the best results reported in the literature left the patient with a greater disability than this man suffers, operation at this time had almost nothing to offer him. This case then illustrates the assistance that lipiodol melography offers in the differential diagnosis of spinal cord tumors and their treatment.

The typical myelogram of intramedullary spinal cord tumor has been recognized by several writers. Mixter[9] calls attention to the significance of the narrow streaks of lipiodol on each side of the spinal canal. Sicard and Forestier[17] state that some intramedullary spinal cord tumors give

pathognomonic myelograms. In Germany, Redlich[13] and Schuster and Markowits,[16] shortly after the introduction of lipiodol, diagnosed intramedullary spinal cord tumors on the basis of myelograms which they considered typical. Heymann[8] reported a characteristic example of such a case. Peiper[11] discusses the myelographic diagnosis of spinal cord tumor and beautifully illustrates the typical and what he considers pathognomonic pictures of intramedullary spinal cord tumor. More recently Porro[12] in Italy and Reiser[14] in Germany have called attention to the characteristic myelograms of intramedullary spinal cord tumors. Except for the paper mentioned above by Mixter, the American literature has been strangely silent on the subject. Occasional cases have been reported without stressing the myelographic appearance.[1] Thus Sachs and Fincher[15] present such a case. Haymaker illustrates the condition in his recent revision of Bing's textbook.[3] Craig[5] gives an illustration, which appears to be typical, but states that the lesion was inflammatory. However, his operative report states that upon splitting the cord dorsally a simple cyst was encountered extending from the fourth dorsal segment to the end of the spinal cord. Globus and Strauss,[7] and others,[6,10] even state that "the oil does not produce a shadow which may be regarded as characteristic of an intramedullary tumor."

CONCLUSIONS

Certain intramedullary spinal cord tumors produce typical and pathognomonic myelograms characterized by a partial block with laterally displaced beaded columns of lipiodol streaking along the vertebral pedicles for several segments. The beading represents the lipiodol in the sheaths of the nerve roots.

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CEREBRAL HEMIATROPHY WITH COMPENSATORY HOMOLATERAL HYPERTROPHY OF THE SKULL AND SINUSES, AND DIMINUTION OF CRANIAL VOLUME*

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THE occurrence of thickening of the cranial vault and overdevelopment of the nasal sinuses on the side of an atrophic brain has been recognized for many years. Peterson and Fisher,[1] in making cranial measurements on 20 patients with infantile hemiplegia, found a diminution in all dimensions of the skull, more particularly on the side opposite the paralysis. Dyke, Davidoff, and Masson[2] made a study of the skull roentgenograms and pneumo-encephalograms of 8 patients with hemiplegia occurring before the age of fifteen months and of one who became hemiplegic at six years. They demonstrated dilatation of the lateral ventricle opposite the hemiplegia, displacement of the ventricle to the atrophic side, thickening of the cranial vault overlying the atrophy, and enlargement of any or all of the ethmoid, frontal, mastoid, and petrous air cells on this side. They explained the changes in the skull as being an effort to compensate for the diminution of normal intracranial growth pressure. It was their impression that the overpneumatization of the sinuses preceded or developed faster than the associated thickening of the skull. Casamajor and Laidlaw[3] later reported another group of 9 cases of hemiplegia associated with convulsions, showing essentially the same changes.

The etiologic factors considered in the 18 previously reported cases were trauma, either natal or postnatal, encephalitis, infectious disease, and cerebral hemorrhage complicating pertussis; in one case the factor was unknown.

Thirty-six patients with hemiplegia and convulsions at the Caro State Hospital for Epileptics form the basis of the present report. An attempt has been made to determine as accurately as possible the immediate cause of the hemiplegia. I concede that in several instances the patient may be misclassified. This error is to be ascribed to two main causes: One is a lack of detailed history concerning the onset of hemiplegia and its associated symptoms; the other is a confessed ignorance of the etiology, in many instances, of acute infantile hemiplegia. The difficulty in determining a definite cause for every acute hemiplegia in infancy is generally recognized. With adequate symptomatology and clinical signs, the diagnosis is not particularly difficult. The catastrophe may accompany acute inflammatory disease of the central nervous system. It may be the complication of an acute infectious disease, such as scarlet fever, pneumonia, or diphtheria. It may occur during a paroxysm of coughing in pertussis. It may complicate otitis media, mastoiditis, septicemia, bacterial endocarditis, purpura, and other blood diseases. It may accompany lead poisoning, degenerative lesions, head trauma, and a number of other conditions.

However, there is a relatively large group of infantile hemiplegia occurring without tangible cause. Ford[4] has described such cases under the title of "acute infantile hemiplegia of obscure etiology." Autopsy in a group of such cases disclosed thick plaques of connective tissue not only in the cerebral but in the visceral arteries,

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DEVELOPMENTAL DISORDER OF CENTRAL NERVOUS SYSTEM

Case	Patient	Sex	Age Yr.	History	Examination	Roentgenograms
1	K.M. No. 2743	M	21	Instrumental delivery. No injury. Left hemiplegia with extensive nevus vasculosus over right half of body since birth. Convulsions since 3 yr.	I.Q. 54. Left side, smaller than right. Left spastic hemiplegia left homonymous hemianopsia, left astereognosis, nevus vasculosus over practically entire right half of body.	Right vault thicker and flatter than left; right half of cranium smaller; right frontal sinuses markedly larger than left; supraorbital cells equal. Calcified mass right mid-frontoparietal area; sinuous calcification right occipital pole. No encephalogram.
2	G.T. No. 2610	F	19	Normal delivery. Last of 11 children. Right hemiplegia noted at birth. Convulsions since 6 yr.	I.Q. 50. Right side hypoplastic. Right spastic hemiplegia, right homonymous hemianopsia, right astereognosis.	Left vault slightly thicker than right; left supraorbital cells moderately overdeveloped; left half cranium smaller. Encephalogram—almost entire left hemisphere replaced by air.
3	C.G. No. 3081	M	22	Retarded mentality noted prior to convulsions with right hemiparesis at 6 mo.	I.Q. 39. Hypoplasia right side. Right spastic hemiparesis.	Left vault slightly thicker than right; left supraorbital cells better developed. No encephalogram.
4	I.L. No. 1893	F	24	Normal delivery. Never mentally normal. Apparently right hemiparesis since infancy. Convulsions since 1 yr.	Idiot. Microcephaly. Right side smaller than left; mild right spastic hemiparesis, right Babinski.	Microcephaly. Left vault slightly thicker than right. Sinuses equal. Encephalogram—generalized brain atrophy, left more marked.
5	R.U. No. 2413	M	12	Normal delivery. Convulsions since 4 mo. old. Left hemiplegia since seizures at 18 mo.	Idiot. Left side underdeveloped. Left spastic hemiparesis. Left Babinski.	Right vault thicker; right supraorbital cells better developed than left; right half cranium smaller than left. Encephalogram—right ventricle considerably dilated with midline structures shifted to right.
6	U.B. No. 3140	M	15	Normal delivery. Convulsions since 4 mo. old. Left hemiparesis since seizures at 10 yr.	I.Q. 47. Left side underdeveloped. Slight left spastic hemiparesis, left hemianesthesia, left Babinski.	Right vault considerably thicker and right supraorbital cells markedly better developed than left. Encephalogram—moderately advanced atrophy, right hemisphere.

INFLAMMATORY DISEASE OF CENTRAL NERVOUS SYSTEM

7	A.W. No. 3121	F	20	Fever and right hemiplegia at 3 mo. Convulsions since 9 mo.	Idiot. Right side smaller than left. "Baby hand" on right. Right spastic hemiplegia with athetosis of fingers.	Left cranial vault slightly thicker than right. Sinuses equal. Encephalogram—marked dilatation of left lateral ventricle; bilateral arachnoid adhesions.

INFLAMMATORY DISEASE OF CENTRAL NERVOUS SYSTEM—(*Continued*)

Case	Patient	Sex	Age Yr.	History	Examination	Roentgenograms
8	F.G. No. 2164	M	17	Meningitis at 7 mo. with left hemiplegia and convulsions.	I.Q. 40. Left side underdeveloped. Left hemiparesis, athetosis left fingers, left Babinski.	No asymmetry of vault or sinuses. No encephalogram.
9	A.G. No. 2976	F	22	"Infantile paralysis" with hemiplegia at 8 mo. Convulsions since 10 yr.	I.Q. 44. Left side hypoplastic. Left spastic hemiparesis with athetosis of fingers and toes. Left Babinski.	Right vault thicker, right supraorbital cells larger, right half of cranium smaller than left. No encephalogram.
10	J.L. No. 2785	M	28	Right spastic hemiplegia and convulsions since infancy.	Imbecile. Right side underdeveloped. Right spastic hemiparesis, athetosis right fingers, right Babinski.	Left vault thicker, left supraorbital cells considerably larger than right. No encephalogram.
11	E.C. No. 2155	F	28	"Infantile paralysis" with left hemiplegia and convulsions at 3 yr.	Left side smaller; left spastic hemiplegia, left hemianesthesia, left homonymous hemianopsia.	Right vault slightly *thinner;* right fronto-ethmoid cells definitely larger than left. Diffuse calcification in dura. Encephalogram—pronounced dilatation of right ventricle; slight dilatation of left. Shift of structures to right.
12	E.F. No. 1765	M	26	Encephalitis lethargica at 12 yr. with convulsions and right hemiparesis.	I.Q. 41. Right arm underdeveloped; lower limbs equal. Right arm spastic, right hemihypesthesia, right homonymous hemianopsia, right Babinski.	Slight thickening left vault; sinuses symmetrical; left half cranium smaller than right. Encephalogram—markedly dilated left ventricle.
13	H.D. No. 2127	M	21	Normal development till "infantile paralysis," right hemiplegia and convulsions at 16 mo.	Idiot. Mild right spastic hemiparesis. Right side underdeveloped. Inactive chorio-retinitis both eyes.	Vaults symmetrical. Left supraorbital cells definitely larger than on right. No encephalogram.
14	G.P. No. 2851	M	21	Hereditary lues. Convulsions at 3 mo. After left-sided paralysis at one year had no seizures till recurred at 15 yr.	Idiot. Hutchinsonian teeth; fixed pupils; primary optic atrophy left eye. Left side underdeveloped. Left spastic hemiplegia with Babinski. Blood and cerebrospinal fluid Kahn negative.	Right vault slightly thicker than left. Sinuses symmetrical. Encephalogram—far advanced atrophy, right hemisphere.

INFLAMMATORY DISEASE OF CENTRAL NERVOUS SYSTEM—(*Continued*)

Case	Patient	Sex	Age Yr.	History	Examination	Roentgenograms
15	V.S. No. 3108	F	27	Hereditary lues. Right hemiplegia during convulsions at 15 mo. Epilepsy since then.	Idiot. Interstitial keratitis. Argyll-Robertson pupils. Right leg smaller. Athetosis right arm and leg. No Babinski. Reflexes equal and overactive. Blood Kahn negative.	Vaults symmetrical and of normal thickness. Supraorbital cells overdeveloped bilaterally. Encephalogram—both lateral ventricles markedly dilated, left more than right.
16	J.E. No. 2576	M	11	Hereditary lues. Meningitis, convulsions, and right hemiplegia at 2 yr.	I.Q. 53. Right side underdeveloped. Right spastic hemiplegia; right homonymous hemianopsia; right Babinski. Blood and cerebrospinal fluid Kahn negative.	Vaults equal. Slight overdevelopment left fronto-ethmoid cells. Encephalogram—tremendous dilatation both lateral ventricles; complete replacement of left hemisphere by air.
17	S.K. No. 1772	M	27	Hereditary lues. Right hemiplegia and convulsions since 8 yr.	Imbecile. Right side hypoplastic. Right spastic hemiplegia; right Babinski. Argyll-Robertson pupils. Blood and cerebrospinal fluid Kahn negative.	Vault and sinuses symmetrical. Encephalogram—pronounced atrophy left hemisphere.
18	P.T. No. 2243	M	29	Hereditary lues. Inadequate history. Convulsions since before 16 yr. Positive Wassermann at 9 yr.	Idiot. Fixed pupils. Right spastic hemiparesis; right Babinski; dystonia right arm. Right side underdeveloped. Blood and cerebrospinal fluid Kahn negative.	Vault and sinuses symmetrical. Encephalogram—pronounced dilatation of left ventricle with shift of structures to left.

COMPLICATION OF NON-CENTRAL NERVOUS SYSTEM INFECTION

19	C.W. No. 2544	M	49	During pertussis at 6 mo. had convulsions and right hemiplegia. Cessation of seizures till 34 yr. when recurred.	Imbecile. Right side underdeveloped. Right spastic hemiparesis and hemihypalgesia; athetosis right fingers.	Left cranial vault slightly thicker than right. Sinuses symmetrical. No encephalogram.
20	D.L. No. 2645	F	16	Bronchitis, fever, right hemiplegia and convulsions at 18 mo.	Right side hypoplastic. Right spastic hemiparesis, hemianesthesia and hemiathetosis.	Left vault considerably thicker; left half of cranium smaller; left frontal sinuses much larger than right; supraorbital cells symmetrical. Encephalogram—left ventricle moderately dilated, structures shifted to left.

TRAUMA TO CENTRAL NERVOUS SYSTEM

Case	Patient	Sex	Age Yr.	History	Examination	Roentgenograms
21	H.R. No. 2844	M	16	Instrumental delivery. Right side paralyzed since birth. Convulsions since 5 yr.	I.Q. 32. Right side smaller than left. Moderate right spastic hemiparesis and ? hypalgesia.	Left vault considerably thicker and left supraorbital cells better developed than right. Encephalogram—advanced atrophy left hemisphere.
22	J.C. No. 2758	M	12	Birth injury with paralysis of right leg. Convulsions since 3 yr.	I.Q. 34. Right spastic hemiparesis, right Babinski.	Symmetrical vault and sinuses. Encephalogram—slight dilatation left ventricle.
23	D.B.	F	20	Precipitate delivery. Convulsions and left hemiplegia two days after birth. Convulsions since 6 yr.	Left side smaller than right; left spastic hemiplegia, hemianesthesia, homonymous hemianopsia. Athetosis left fingers, astereognosis left hand.	Right vault *thinner* than left. Right half of cranium smaller than left. Sinuses symmetrical. Encephalogram—large porencephaly right hemisphere; structures shifted to right.
24	E.P. No. 1364	M	29	When 2 days old had "peculiar spells" and right-sided paralysis. Probable birth injury. Convulsions since infancy.	Idiot. Right side underdeveloped. Right spastic hemiplegia. Right Babinski.	Vaults symmetrical. Marked overdevelopment of left supraorbital and petrous cells. Encephalogram—very extensive dilatation of left ventricle; considerable dilatation of right ventricle.
25	C.C. No. 1434	M	31	Head injury at 1½ yr. Unconscious 4 days. Right hemiplegia and convulsions since injury.	Moron. Right side underdeveloped. Spastic right hemiparesis; athetosis right fingers and toes.	Left vault considerably thicker; sinuses about equal. Encephalogram—moderate, generalized atrophy left hemisphere. Structures shifted to left.
26	W.K. No. 2596	M	24	Head injury at 7 yr. unconscious 1½ hr.; 19 convulsions. Seizures recurred at 10 yr. and right hemiparesis noted.	Right side underdeveloped; right spastic hemiparesis, hemianesthesia, homonymous hemianopsia, mixed aphasia.	Left vault slightly thicker; sinuses equal. Encephalogram—moderate, generalized dilatation left ventricle; structures shifted to left.

ACUTE HEMIPLEGIA OF OBSCURE ETIOLOGY

27	M.B. No. 2832	F	18	Fever, convulsions, and right hemiplegia at one year. Generalized and right jacksonian sensory seizures since 14 yr.	I.Q. 66. Right side hypoplastic. Right spastic hemiplegia; right hemianesthesia.	Left cranial vault markedly thicker than right; left supraorbital cells extensively overdeveloped. Encephalogram—marked dilatation left lateral ventricle, structures shifted to left.
28	J.G. No. 1820	M	31	Instrumental delivery without difficulty in resuscitation. Right hemiplegia and convulsions since 1 yr.	Imbecile. Right side underdeveloped. Right spastic hemiparesis.	No asymmetry of skull or sinuses. No encephalogram.

ACUTE HEMIPLEGIA OF OBSCURE ETIOLOGY—(*Continued*)

Case	Patient	Sex	Age Yr.	History	Examination	Roentgenograms
29	A.K. No. 2396	M	25	Instrumental delivery without difficulty in resuscitation. Right sided weakness since 15 mo. Convulsions since 5 yr.	I.Q. 67. Right side underdeveloped. Mild right spastic hemiparesis; right Babinski; athetosis right fingers.	Left vault slightly thicker; left supraorbital cells slightly larger than right. Encephalogram—moderate, generalized brain atrophy, greater on left.
30	C.R. No. 1927	M	35	Developed normally until sudden convulsions and left hemiplegia at 16 mo.	Moron. Left side hypoplastic. Left spastic hemiplegia and hemianesthesia.	Right vault considerably thicker; right frontal and supraorbital cells markedly larger than left. No encephalogram.
31	G.M. No. 533	M	37	Normal delivery. During "teething convulsions" at 18 mo. developed right hemiplegia.	Idiot. Right side hypoplastic. Right spastic hemiplegia.	Left cranial vault thicker and left half of cranium smaller than right. Sinuses equal. No encephalogram.
32	C.W. No. 3181	M	31	Developed normally until sudden right hemiplegia at 4 yr. Convulsions since 12 yr.	Moron. Right side underdeveloped. Right hemiparesis and slight hemihypalgesia. No Babinski.	Left vault thicker and left supraorbital cells considerably larger than right. Encephalogram—very marked dilatation of left ventricle, moderate dilatation of right. Structures shifted to left.
33	A.T. No. 2889	F	29	Developed normally until sudden left hemiplegia at 4½ yr. Convulsions since 5 yr.	I.Q. 64. Left side hypoplastic. Left spastic hemiplegia, hemianesthesia, homonymous hemianopsia.	Right vault slightly thicker than left. Right supraorbital, petrous, and mastoid cells considerably better developed than left. Encephalogram—right ventricle markedly dilated; structures shifted to right.
34	F.H. No. 2041	F	20	Sudden right hemiplegia with convulsions at 5 yr.	I.Q. 91. Right side underdeveloped. Right spastic hemiparesis and hemianesthesia.	No asymmetry of vaults or sinuses. No encephalogram.
35	M.S. No. 992	F	30	Apparently normal until convulsions at 6 yr. with temporary right hemiparesis. Permanent right hemiplegia during seizures at 16 yr. Right jacksonian motor attacks.	Right side smaller than left. Right spastic hemiplegia, hemianesthesia, right homonymous hemianopsia.	Pronounced thickening left cranial vault; marked overdevelopment left supraorbital cells. No encephalogram.
36	G.W. No. 223	M	47	Developed normally until convulsions and right hemiplegia at 6 mo.	Imbecile. Right side hypoplastic. Right spastic hemiplegia.	Left vault slightly thicker; left half cranium smaller than right; sinuses equally well developed bilaterally. Encephalogram—both lateral ventricles dilated, left much more than right. Structures shifted to left.

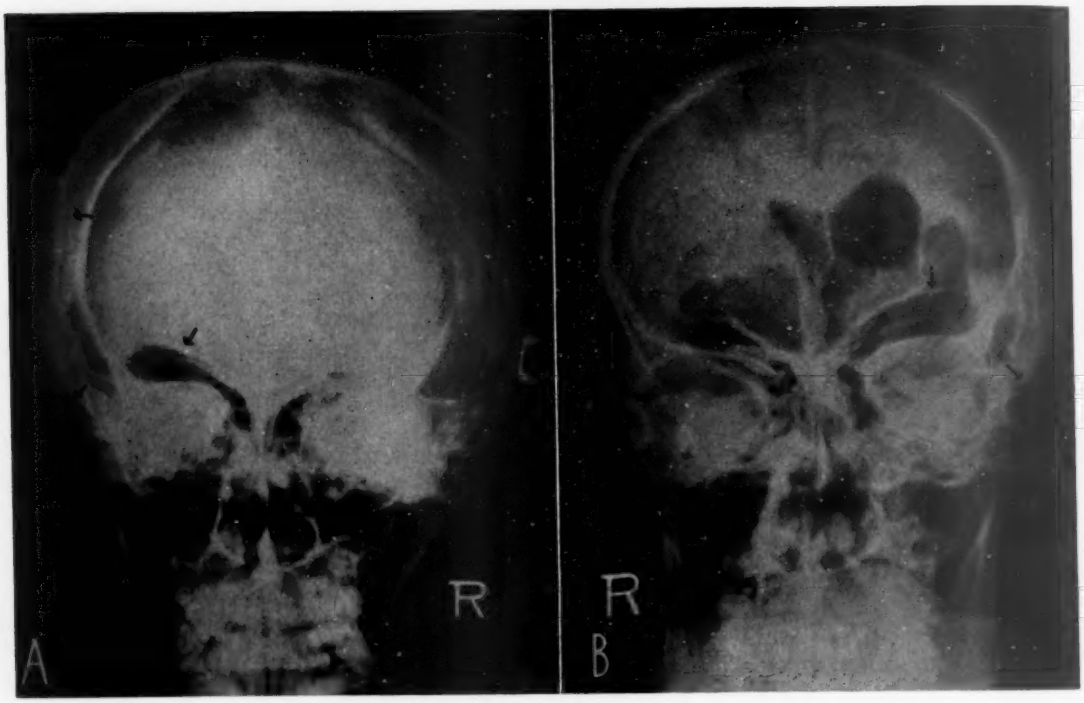

Fig. 1, *A* and *B*. Case 27.

Fig. 2, *A* and *B*. Case 6.

atrophy of the muscular layers of the media, fragmentation of the elastic lamellae, and thrombi in various cerebral arteries. There was nothing to suggest an inflammatory process nor were there signs of syphilis. The cause of the changes in the visceral and cerebral arteries remained obscure. He found no anatomical evidence to support the theory of Strümpell and Marie that such cases represent the cerebral localization of the virus of epidemic poliomyelitis. Of the 36 cases in this report, 10 are placed in this classification, while in the remainder the cause of hemiplegia is more definitely ascertained.

A review of the accompanying case records shows that 25 of the 36 individuals developed their hemiplegia before the second year, 7 between the second and seventh, and 4 between the eighth and thirteenth years. There are 24 instances of thickening of the cranial vault of varying degree, 19 of overdevelopment of the nasal sinuses—usually the supraorbital air cells, and 9 in which the affected side of the skull is smaller in volume than its counterpart. Neither sex nor etiology of the hemiplegia seems to be of significance in the skull and sinus alterations, or in the amount of demonstrable brain atrophy.

By the observation of these asymmetrical changes on routine skull films, one may often, without seeing the patient, designate the side on which he is paralyzed. A good illustration of homolateral thickening of the vault and overdevelopment of the supraorbital and mastoid air cells accompanying a cerebral hemiatrophy with shift of midline brain structures to the atrophic side is seen in Figure 1, *A* and *B* (Case 27).

While the thickening of the vault and hypertrophy of the sinuses are usually roughly correlated with the amount of underlying brain atrophy and early age of onset of hemiplegia, exceptions at times occur. Case 6 (Fig. 2, *A* and *B*) whose hemiparesis occurred at ten years illustrates this rather well. His encephalogram shows only a moderate degree of brain atrophy, yet the homolateral bony changes

Fig. 3. Case 24.

are quite distinct. They consist of diminution of cranial volume, thickening of the vault, and overpneumatization of the supraorbital, mastoid, and petrous air cells.

By reference to the case records it can readily be seen that not every instance of cerebral hemiatrophy, no matter of what degree, is accompanied by the described asymmetry of the vault and sinuses. Likewise there are instances in which only the vault or only the sinuses show any alteration of the nature under consideration, even in the face of considerable brain atrophy (Fig. 3, Case 24). Nevertheless these asymmetrical skull changes occur frequently enough that when confronted by them in routine skull films, one is warranted in voicing a suspicion of underlying brain atrophy.

Although the most common change in the vault is thickening, in 2 instances (Cases 11 and 23) the skull overlying the

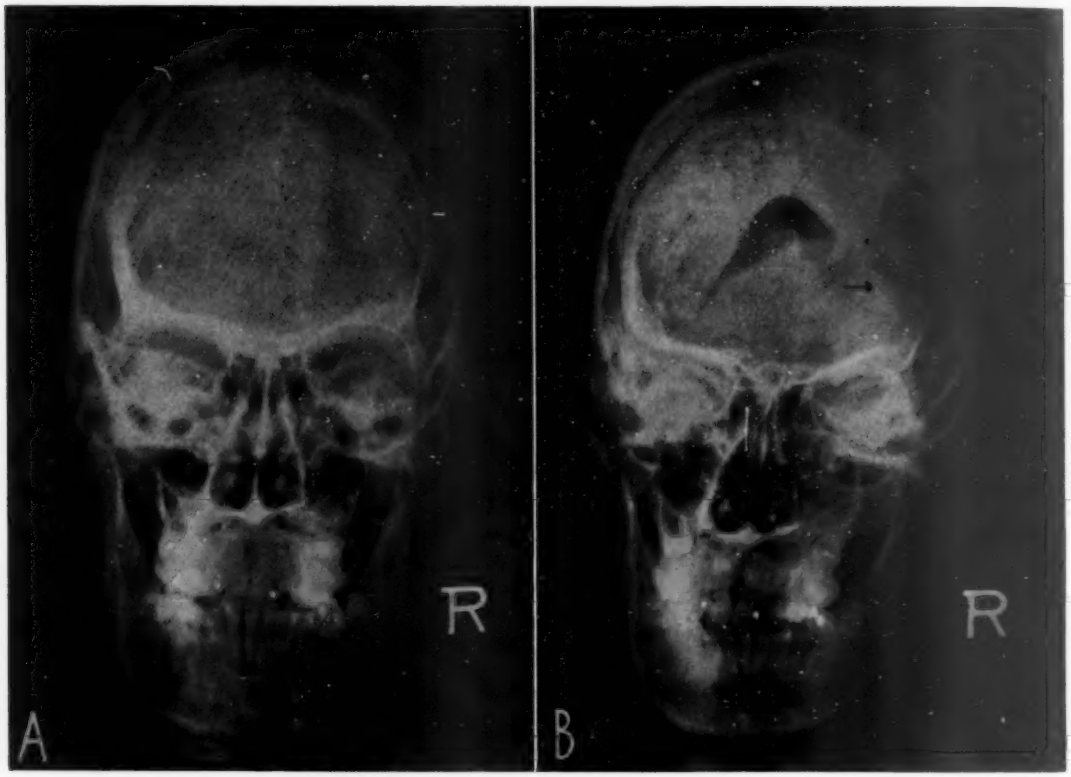

Fig. 4, *A* and *B*. Case 23.

Fig. 5.

affected brain is thinner than its counterpart. In one of these patients the frontoethmoid cells on the affected side of the brain are overdeveloped while in the other the sinuses are about equally well pneumatized. Figure 4, *A* and *B* (Case 23), illustrates this thinning of the overlying vault and the presence of marked homolateral brain atrophy with shift of midline structures towards the atrophic side. The thinning of the vault is probably in the nature of a pressure atrophy, although it is difficult to see why this type of asymmetry should occur in some skulls and thickening occur in the majority.

Since unilateral brain atrophy is so often associated with homolateral skull and sinus changes, one might expect that with bilateral cerebral atrophy, there would be thickening of the vault and overpneumatization of the sinuses on both sides of the skull. To determine this, the skull films of 21 patients without hemiplegia whose encephalograms demonstrated marked bilateral cerebral atrophy were compared

with the films of hemiplegics. Most of these patients were examples of cerebral agenesis, a few of whom exhibited tetraparesis. However, only 2 showed thickening of the cranial vault and this was bilateral (Fig. 5).

It appears, therefore, that if the intracranial growth pressure is equally distributed, the vault and sinuses develop in a symmetrical manner even though there may be considerable underlying brain hypoplasia or atrophy. On the other hand, if there is an imbalance of such intracranial growth, as in hemiatrophy of the brain, homolateral compensatory changes in the skull will be likely to occur. These are exhibited as alterations in width of the vault, usually a thickening, but in some instances a thinning, overpneumatization of the accessory sinuses, and diminution of cranial volume.

CONCLUSIONS

1. In a significant proportion of instances of hemiplegia occurring in early years roentgenograms show thickening of the cranial vault, overpneumatization of the accessory sinuses, and diminution of cranial volume on the side corresponding to the brain defect.

2. Pneumo-encephalograms demonstrate varying degrees of atrophy of the underlying brain.

3. Occasionally the vault overlying a pronounced cerebral hemiatrophy is thinner rather than thicker.

4. The skull changes, degree of brain atrophy, and age of onset of hemiplegia are roughly correlated.

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LESIONS OF THE LUNGS IN THE LYMPHOMATOID DISEASES*

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THE literature, especially of the past two decades, contains numerous references to pulmonary lesions representing invasion of the lung tissue by the various lymphomatoid diseases. References to lesions of the lung in Hodgkin's disease seem to be considerably more numerous than references to such lesions as part of lymphosarcoma or leukemia. In fact, Versé[19] in 1931 stated that the evidence indicated that in perhaps 10 per cent or more of cases of Hodgkin's disease the disease process actually begins within the lung substance. Terplan,[17] however, in 1922, stressed the rarity of primary Hodgkin's disease of the lung. In 1934, Moolten[12] reported 9 cases of Hodgkin's disease with lung lesions of various types. He believed that his Case 8 was an example of primary pulmonary Hodgkin's disease. This case showed lesions that were largely peripheral, pleural and subpleural, while the spleen showed only a diffuse hyperplasia without nodule formation.

INCIDENCE

A study of material at the Mayo Clinic by Kirklin and Hefke[10] in 1931 showed that intrathoracic lesions, including mediastinal as well as pulmonary, were found in about 50 per cent of their cases of Hodgkin's disease, in about 20 per cent of their cases of lymphosarcoma, and in about 20 per cent of their cases of leukemia. These authors found that whenever involvement of the thorax was demonstrable roentgenographically, there were lesions of the lungs in 30 per cent of the cases of Hodgkin's disease, in 23 per cent of the cases of lymphosarcoma, and in 40 per cent of the cases of leukemia. These figures would appear to indicate the following incidence of lung lesions: 15 per cent in Hodgkin's disease; 4.6 per cent in lymphosarcoma; 8 per cent in leukemia.

Reports of the incidence of lung lesions of these diseases were made by Falconer and Leonard[6,7] in 1936 and 1938, as follows: Hodgkin's disease, 37.6 per cent; lymphosarcoma, 36 per cent; lymphatic leukemia, 30 per cent. Cutler found pleural or lung lesions in lymphosarcoma in 33 per cent.

Versé thought that the aggressive type of Hodgkin's disease, likely to produce tumor-like infiltrations in the lung, is found mostly in persons twenty to forty years of age. He estimated that in those who die of Hodgkin's disease involvement of the lungs is found in about 33 per cent. He emphasized that there is no specific roentgen picture of Hodgkin's disease in the lung and quoted Held's statement that the picture is typical by reason of its protean features.

Lenk[11] stated that it is so unusual for lymphogranulomatous nodes to cause phrenic nerve paralysis that the discovery of such paralysis on roentgen examination of the chest speaks against a diagnosis of lymphogranulomatosis.

Another diagnostic point mentioned by Lenk, which seems worth remembering in connection with the clinical diagnosis of intrathoracic Hodgkin's disease, is that the clinical picture of tuberculosis in conjunction with the roentgen picture of malignant lung tumor speaks for a diagnosis of Hodgkin's disease.

TOPOGRAPHIC CLASSIFICATION

Various classifications of types of intrathoracic lesions of the lymphomas have been suggested by different authors, particularly for Hodgkin's disease. Wessler

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and Greene[21] reported a study of intrathoracic Hodgkin's disease in 25 cases. They found some involvement of the nodes or other lymphatic tissue within the chest in all, and described 4 types:

(1) Mediastinal tumor, 8 cases.

(2) Infiltrative type, with invasion of neighboring lung. They expressed doubt as to whether this type represents a true invasion or whether it might mean a transformation of intrapulmonary lymphoid tissue into granuloma. There were 4 cases in this group.

(3) Isolated nodules or metastases in lung, invariably accompanied, however, by lymphomatous masses at the roots of the lungs. This type was found in 4 cases, always in association with one of the other types. They regarded the nodules as autochthonous foci developing in pre-existing pulmonary lymphoid tissue.

(4) Discrete nodules at the roots, 17 cases. Presenting faint, homogeneous, lobulated shadows, this type most commonly was found by them represented by an enlargement of the right paratracheal group of nodes, causing an oval shadow in the right upper mediastinum. This site, they stated, was seldom affected by lymphadenopathy of other pulmonary or mediastinal tumors, or of tuberculosis of adults. (However, they stated in infants and children with tuberculosis the right paratracheal nodes are more commonly affected.)

According to Moolten, the simplest anatomic grouping for Hodgkin's disease in the lung is that of Ceelen and Rabinowitsch, namely: (1) generalized, (2) more localized.

Versé[19] described 5 groups of Hodgkin's lesions in the lung:

(1) Mediastinobronchial node lesions with direct invasion of the lung.

(a) by the way of the hilum.

(b) through the medial surface of the lung.

Table I

PERCENTAGE INCIDENCE OF PULMONARY LESIONS IN LYMPHOMAS

Authors		Hodgkin's Disease	Lympho-sarcoma	Leukemia	Mycosis Fungoides
Kirklin and Hefke[10]	(roentgen examination)	15	4.6	8	—
Versé[19]	(autopsies)	33	—	—	—
Moolten[12]	(autopsies)	50	—	—	—
Falconer and Leonard[6,7]	(roentgen and autopsy examination)	31	36	30	—
Memorial Hospital 1940	(roentgen examination)	34	12	11	30
	(autopsies)	64	39	—	—

(2) Mediastinobronchial node lesions with peri- and intrabronchial spread.

(3) More or less lobar (diffuse) infiltration of the lung, with varying degrees of involvement of the bronchomediastinal nodes.

(4) Confluent lobular (isolated circumscribed) focal formations with involvement in varying degrees of the bronchomediastinal nodes.

(5) Miliary (lymphohematogenous) foci with involvement in varying degrees of the bronchomediastinal nodes.

Moolten suggested another classification of Hodgkin's disease in the lung, based on 18 autopsied cases at Mt. Sinai Hospital in New York. In this group 9 cases, or 50 per cent, had lung lesions and in 2 cases he found lesions within the mucosa of the trachea and bronchi. His classification was as follows:

(1) Granulomatous pan-bronchitis and bronchopneumonia (peribronchial form of granulomatous interstitial pneumonia).

(2) Granulomatous pleurogenous pneu-

monia (pleurogenous form of granular interstitial pneumonia).

(a) primary pleurogenous (rare) (his Case 8).

(b) secondary (invasion from adjacent infiltrated structures, such as the mediastinum).

(3) Exudative lobar and lobular pneumonia.

(a) acute (gelatinous pneumonia).

(b) subacute and chronic (organizing).

(4) Miliary, submiliary, and multiple isolated nodular foci (hematogenous, lymphogenous).

Lenk[11] made the following classification of intrathoracic Hodgkin's disease:

(1) Hilar node involvement, occasionally going through capsule and infiltrating lung.

(2) Widespread small or large nodules (miliary and submiliary).

(3) A rare form—solitary or multiple large nodules, apparently arising from lymph nodes of the lung. This form may necrose centrally.

(4) Rarest form of all—originating in bronchial mucosa, growing, and causing stenosis. Such a type may exist without enlargement of intrathoracic lymph nodes.

ENDOBRONCHIAL AND INTRA-ALVEOLAR HODGKIN'S DISEASE

Moolten stressed the tendency of Hodgkin's disease to involve the lung not only by extending along the bronchi by a peribronchial route, but also by intrabronchial granulomatous organization of fibrin plugs. The term pan-bronchitis, used by some authors, involves a combination of granulomatous bronchitis and peribronchitis, of lymphadenitis and perilymphadenitis. Moolten lists the following modes of granulomatous invasion of the alveoli: (1) through the natural air passages; (2) specific granulomatous organization of masses of retracted fibrin strung from alveolus to alveolus; (3) organization of fibrin, first by fibroblasts of ordinary type, only subsequently assuming the aspects of lymphogranulomatous tissue.

A point of interest histologically in this connection is Moolten's observation that in the pulmonary alveoli the Hodgkin's process has an opportunity to grow in "pure" fashion, unhampered by stroma and other tissue elements, and that the "pure lesion" is seen to be a specific cell mixture. Thus fibroblastic transformation and dense scarring can be regarded as probably specific phases of Hodgkin's disease.

While several authors have described plaques, elevated areas or even bulky nodular outgrowths of lymphogranulomatous tissue on the mucosa of the bronchi, Moolten found in his Case 5 a polypoid tumor measuring $4 \times 2 \times 1$ cm. in the right main bronchus, and stated that no such case had previously been reported.

Such lesions seen bronchoscopically would not readily be diagnosed clinically as Hodgkin's disease unless that diagnosis had already been established by histologic section. Lenk's rarest form, originating in bronchial mucosa and causing stenosis without involvement of nodes, would particularly cause difficulties in diagnosis. In fact, the differential diagnosis between Hodgkin's disease and bronchial carcinoma is in not a few instances extremely difficult. Hurd[9] in 1922 reported a case in which the histologic diagnosis of Hodgkin's disease was made by bronchoscopic biopsy.

As one point in the clinical differentiation between Hodgkin's disease of the lung and bronchial carcinoma, Moolten notes the rarity of an expansile tendency in Hodgkin's nodules in the lung. Thus, atelectasis, he says, is rare except as a result of some special event, such as massive effusion or bronchial occlusion.

CAVITATION OF LUNG IN HODGKIN'S DISEASE

Cavitation is not a common feature of Hodgkin's disease of the lung, yet it has been observed and reported by many writers, even as long ago as 1888 (Claus,[3] quoted by Versé) and 1904 (Yamasaki[22]). Not infrequently the recognition of a cav-

ity or cavities in the lung in cases of Hodgkin's disease has led to an erroneous clinical diagnosis, such as tuberculosis, carcinoma, congenital cysts (case of Radauskas[15]). Cavitation has been found varying from areas of central necrosis in small nodules in the lung to huge cavities—perhaps the largest having been reported by Weber.[20] In his Case 5, in a male, aged thirty-eight, autopsy showed a cavity the size of a child's head in the right upper lobe, communicating through an opening 2 cm. in diameter, with another cavity the size of a fist in the right lower lobe. Weber found no evidence of tuberculosis. While in some instances tuberculosis has been coexistent and has led to cavity formation, and in other instances cavities may have arisen as a result of irradiation together with infection, or as a result of bronchial occlusion and infection, it would seem from the literature that cavitation can occur in Hodgkin's nodules in the lung as a spontaneous process without the influence of extraneous factors. In Dvorak's case in which the patient died of hemorrhage resulting from erosion between the left common carotid artery and the esophagus, there was an apple-sized cavity in the right lung.

TRACHEO-ESOPHAGEAL FISTULAE IN HODGKIN'S DISEASE

A Finnish writer, Pesonen,[14] described in 1938 a case of lymphogranulomatous fistula between trachea and esophagus, demonstrated roentgenographically by lipiodol and also by autopsy. Pesonen stated that he had been unable to find mention in the literature of such fistulae in Hodgkin's disease. However, Weber had reported such a case (his Case 7) eight years previously, and Radauskas states that bronchial fistulae may be formed, although he does not state with what organs the bronchial fistulae communicate.

The Memorial Hospital series contains at least one case of tracheo-esophageal fistula confirmed on autopsy. In another case, a fistula was thought to have been demonstrated by spillage of barium into the bronchial tree, but no fistula could be seen on esophagoscopy, and the spillage of barium may have occurred because of defective swallowing accompanying recurrent nerve paralysis.

There is rather general agreement that the response of infiltrations in the lung caused by Hodgkin's disease is somewhat less satisfactory than is the case with many other lesions of the disease. Desjardins,[4] for example, stated that the diffuse parenchymatous infiltrations of the lungs and the symptoms that attend such infiltration generally subside after irradiation, but that in his experience the infiltrate never subsides completely.

It is probably true that the depth of some of the lung lesions and the character of their tissue environment are important factors in their tendency to decreased response to irradiation, in contrast to similar granulomatous lesions in other sites.

Peirce, Jacox and Hildreth[13] noted spontaneous regression of an apparently widespread pulmonary infiltration in one case after several transfusions, and without the use of any irradiation.

LUNG LESIONS IN LYMPHOSARCOMA AND LEUKEMIA

One finds in the literature considerably fewer references to pulmonary lesions of lymphosarcoma and leukemia than to those of Hodgkin's disease. It is difficult to see why this should be the case as far as the few reports of comparative figures on incidence of pulmonary lesions in these three diseases are concerned, as the frequency of occurrence of lung lesions in lymphosarcoma and leukemia seems to be of about the same order as in Hodgkin's disease. Perhaps the greater controversy about the nature of Hodgkin's disease has generally excited more interest in a clinical study of its features.

Falconer and Leonard[6] found lesions of the lung in 31 per cent of their cases of Hodgkin's disease and, adding 7 other cases from the literature, making a total

of 125 cases studied, obtained an incidence of 37.6 per cent. In lymphosarcoma they[7] found lung lesions in 36 per cent, and in lymphatic leukemia in 30 per cent. Cutler found pleural or lung lesions in 33 per cent of cases of lymphosarcoma.

Falconer and Leonard found all of Versé's types of lung involvement (described for Hodgkin's disease) represented among their cases of lymphosarcoma and lymphatic leukemia except that in 11 cases of lymphosarcoma there was no example of Versé's Type IV (confluent lobular, isolated, circumscribed, focal formations with involvement in varying degrees of the bronchomediastinal nodes). Pleural effusion was common in their cases—in 7 of 11 cases of lymphatic leukemia, and in 8 of 12 cases of lymphosarcoma. They found that cases with massive pleural effusion did not respond well to roentgen therapy.

We have found in the literature no report of cavitation or of bronchial fistula in lymphosarcoma or leukemia.

In regard to lymphosarcoma of the lung, Lenk stated that retraction of the lung (as noted so frequently in carcinoma) has not so far been described.

Leukemic tumors in the lungs were classified by Lenk as: (1) tumors of the hilar nodes; (2) scattered leukemic foci in the lungs. He makes a point in regard to differential diagnosis in that in leukemia one may see a regression of leukemic tumors in lung (or elsewhere) following irradiation of another part of the body, and states that this "Fernwirkung" is not seen in Hodgkin's disease, tuberculosis, or lymphosarcoma. Such an effect, he says, may be of considerable diagnostic importance in aleukemic forms of leukemia.

INCIDENCE IN MEMORIAL HOSPITAL CASES

As far as our material at Memorial Hospital is concerned, this report must be regarded as a preliminary one, as time has not permitted more than a cursory survey of our cases. The topic seems well worth further study and a more extended report, comprising a broader review of the literature and a more nearly complete review of our cases.

We have very briefly reviewed the following material:

(1) Hodgkin's disease (verified by biopsy or autopsy) since January 1, 1930, including records of 224 patients dead or lost to follow-up and of 73 current cases; also autopsy records in 28 cases of the past ten years.

(2) Lymphosarcoma (verified by biopsy or autopsy) from 1918 to 1938, including 196 cases, upon which a study of end-results was recently published by Sugarbaker and Craver;[16] also autopsy records in 23 cases of the past ten years.

(3) Leukemia (verified by autopsy, biopsy, or blood count and clinical course) including records of 195 patients dead or lost to follow-up from January 1, 1930 to May, 1940. There were 146 cases of lymphatic leukemia, including 7 acute cases, and a considerable proportion of aleukemic cases or ones with relatively low total white cell counts throughout. There were only 48 cases of myelogenous leukemia including 2 acute cases and 3 examples of erythroleukemia. In addition, there was one case of monocytic leukemia occurring terminally in Hodgkin's disease.

(4) Mycosis fungoides (verified by biopsy) including records of 13 patients dead or lost to follow-up from January 1, 1930, to May, 1940.

In Hodgkin's disease a survey of the records of 224 patients dead or lost to follow-up since January 1, 1930, and of 73 current cases and excluding 15 cases in which no roentgen film of the chest was made shows an incidence of lung infiltrations or nodules of 34.0 per cent. A review of autopsies for Hodgkin's disease in the past ten years, 28 in number, shows a total of 21 cases, or 75 per cent, having pleuropulmonary lesions, including effusions; and definite nodular or infiltrative lung or pleural lesions in 18 of 28 cases, or 64.3 per cent.

One case that came to autopsy in 1936,

a woman, aged thirty-four, had a tracheo-esophageal fistula with bilateral lung abscesses, in addition to generalized Hodgkin's disease with marked enlargement of mediastinal nodes, diffuse involvement of both lungs, and of the spleen and liver. Microscopically there was apparently a diffuse peribronchial Hodgkin's process merging into the effects of the suppuration resulting from the tracheo-esophageal fistula, and it was impossible to separate the organizing pneumonitis from the fibrosis of Hodgkin's disease.

In 5 of the 18 autopsied cases in which there were Hodgkin's lesions in the lung, evidence of tuberculosis was also found either in the lung or in tracheobronchial nodes. In 2 cases, old calcareous and caseous tuberculosis was found in the tracheobronchial nodes; in one case, an old healed lung lesion was found; and in 2 cases there was intimate fusion of typical tubercles and Hodgkin's disease in the lungs.

In one case of Hodgkin's disease, a terminal leukemia, apparently monocytic, had produced a leukemic infiltration of vessels and air vesicles in the lungs.

Once case showed an acute miliary Hodgkin's granulomatosis of the lungs as well as of the spleen and liver, while there was chronic fibrosing Hodgkin's disease in the lymph nodes and bone marrow.

In 5 of the 18 autopsied cases showing lung or pleural lesions the microscopic examination showed Hodgkin's sarcoma.

In lymphosarcoma, a study of 196 cases from 1918 to 1938 by Sugarbaker and Craver gave an incidence for a group of lesions broadly classified as pleuropulmonary of 12 per cent. A recent survey of autopsy material of the past ten years showed some type of pleural or pulmonary involvement, including effusions, in 14 of 23 cases, or 60.9 per cent, and definite lung or pleural nodules or infiltrations in 9 of 23 cases, or 39.1 per cent.

In the 13 cases of mycosis fungoides, chest films had been made in all, and there were 4 instances of nodular or infiltrative lesions in the lungs, or 30 per cent.

In the 195 leukemias, one or more chest films had been made in 135 cases. Evidence of mediastinal widening was found in 39, hilar accentuation in 46, thickened pleura in 20, peribronchial thickening in 16, and some infiltration in the lung, usually rather minimal, in only 16. Thus, in this material we have a percentage of only 11.8 of those cases in which chest films were made, with roentgen evidence of some lung change other than mere pleural thickening or peribronchial infiltration. It is our impression that, in general, these changes are not well marked, that they are seen much more commonly in lymphatic than in myelogenous leukemia, and that in chronic lymphatic leukemia, aside from mediastinal widening, what we expect to find most commonly, if anything, in the chest film is some degree of hilar and possibly peribronchial thickening of questionable interpretation.

SUMMARY

1. Lesions of the lung in the lymphomatoid diseases are probably much more common than is generally believed.

2. Their form is extremely variable.

3. They may be very radiosensitive, yet partly perhaps because of their depth and the character of their tissue bed they are not so easily controlled by irradiation as are some other manifestations of these diseases.

4. Cavitation in the center of specific granulomatous masses in the lung may occur in Hodgkin's disease.

5. Tracheobronchial fistulae may occasionally be found in Hodgkin's disease.

6. The pulmonary lymphomatous lesions may be rather silent clinically, and not detectable by physical signs. Therefore, a plea is entered for more frequent roentgen examination of the chest in the care of patients suffering from the lymphomatous diseases.

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DISCUSSION

DR. HARRY HAUSER, Cleveland, Ohio. I have just been called upon this morning to discuss this subject because of the fact that two collaborators and myself have analyzed a group of 91 cases of Hodgkin's disease at the Cleveland City Hospital as related to intrathoracic involvement. We have analyzed some 91 cases, diagnosed either by biopsy or autopsy, including roentgen examination of the chest. About 60 per cent of these cases showed involvement somewhere in the chest.

Our classification is a modification of Wessler and Greene's, which Dr. Craver has mentioned in his paper, and is somewhat as follows: (1) mediastinal types, including the paratracheal lymph nodes; (2) hilar node type; (3) infiltrative type including bronchopneumonic distribution; (4) nodular type, miliary nodules, large solitary or multiple nodules; (5) pleural involvement type, either secondary pleural effusion or direct invasion of the pleura; and (6) at the suggestion of Dr. Craver, bony involvement type.

We had one patient in our series with sternal involvement. In one of our infiltrative cases there was multiple cavitation in the right upper lobe. The appearance was quite similar to that of pulmonary tuberculosis.

I might say in differential diagnosis that the two main diseases to differentiate from intrathoracic Hodgkin's disease are tuberculosis and carcinoma of the bronchus.

We found no cases with tracheobronchial fistula in our group of Hodgkin's disease. We do not believe that the depth of the lesion makes any difference as to the irradiation response. It is my opinion that the inherent biological factors probably play a rôle.

The great majority of our patients showed a definite response to irradiation in the form of regression. There were a few, however, who showed no regression whatsoever, even though large total doses of fractionated radiation were given.

We are in agreement with Dr. Craver in that intrathoracic lesions are more common than was previously thought. We also agree that manifestations or morphology are variable and that many lesions fail to give symptoms and are discovered only by a roentgenogram of the chest.

Dr. Milton Friedman, New York City. I would like to ask Dr. Craver if he saw any case of Hodgkin's disease in which he felt the cavitation was spontaneous in nature.

Dr. Craver (closing). In answer to Dr. Friedman, I think we found no case with cavitation in which we thought it was really spontaneous, that is, occurring as a spontaneous breakdown within a Hodgkin's nodule. There was always some reason, such as bronchial occlusion plus infection, tracheo-esophageal fistula or something of that sort that accounted for it. But from the literature, I judge there is evidence that necrosis and caseation, causing cavitation, can occur spontaneously in Hodgkin's nodules in the lung whether they are small or large.

One point which I didn't have time to bring out is that one finds in the literature reference to intrabronchial organization of fibrin plugs into granulomatous tissue and the onset of Hodgkin's disease within trachea or bronchi as plaques or polypoid outgrowths which may occur without any involved nodes, either externally or internally. Those cases, of course, are not recognized bronchoscopically as being Hodgkin's disease; one must await the biopsy to show the real nature of the disease.

Dr. Lee Hurd, a rhinologist of this city, about 1922 made a bronchoscopic diagnosis of Hodgkin's disease—the diagnosis based on the bronchoscopic biopsy which he had made.

I do agree with Dr. Hauser that there probably is something inherent in the tissue bed in the lungs which also accounts for the lack of as good response in these lesions as in many of the other manifestations of the disease.

ROENTGENOSCOPY AS A DIAGNOSTIC AID IN CORONARY OCCLUSION

A STUDY OF 164 CASES*

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THE prevalence of coronary occlusion is becoming more widely recognized as methods of diagnosis improve. It has been estimated that at least 500,000 attacks occur annually.[9] Yet many of these escape detection, even in the acute stage, because they are associated with little or no pain. Also in many cases the diagnosis cannot be made following recovery because the electrocardiogram has become normal. It is in these cases particularly that roentgenoscopy is valuable as a means of detecting the myocardial infarction. During the past five years I have found this method reliable; it is simple and inexpensive, and should form part of the examination of every suspected case of coronary occlusion.

Roentgenoscopically, a localized systolic expansion of the left ventricular border is considered characteristic, if not pathognomonic, of myocardial infarction due to coronary occlusion. It is found in 50 per cent of cases, whether examined early or late after the attack. Systolic expansion or reversal of pulsation has been described in cardiac aneurysm,[2,3,4,10] but prior to the observations of myself[6] and my associates,[7,8] it has not been reported following occlusion with infarction alone. In the latter condition, only diminution or absence of pulsation has been noted,[5] which may be present in other types of heart disease.

MATERIAL USED

Roentgenoscopic examinations were made of 300 patients seen in private practice since 1934. Of these 164 had suffered a coronary occlusion, and the remaining 136, who served as controls were grouped as follows: 41 having coronary disease without occlusion; 26, hypertension; 27, chronic rheumatic valvular disease; and 42 normal hearts.

TECHNIQUE

For a distinct view of the cardiac pulsations it is necessary for the eyes to become thoroughly accommodated, five to ten minutes usually sufficing. A general survey of the heart and lungs is made first in the posteroanterior view, as in routine roentgenoscopy. The patient is then instructed to hold his breath, without straining, after a moderately deep inspiration. The opening of the roentgenoscopic screen having been reduced to the area of the left cardiac border, attention is focused on the time relation between the aortic and ventricular pulsations. Normally these are opposite in phase: as the left border of the ventricle contracts in systole, the aorta expands. The inthrust of the upper portion of the left ventricle usually precedes slightly that at the apex. As the apex moves inward, the diaphragmatic surface is elevated.

The posteroanterior view is usually the most satisfactory for observing the ventricular contractions. In order to study those of the lateral and posterior walls of the left ventricle, the heart is also examined in the left oblique and left lateral positions.

When the breath is held without strain during roentgenoscopy the heart rate is slowed and the movements of the diaphragm eliminated, both of which help to delineate the cardiac pulsations. The advantage is lost, however, by forcibly holding the breath; strain raises the intrathoracic pressure, which reduces cardiac output by decreasing the venous return to the heart. Also, there is external pres-

* Presented in part before the New York Roentgen Ray Society at the New York Academy of Medicine April 17, 1939.

sure on the ventricles. As a result the ventricular pulsation may be abolished or diminished.

TYPES OF ABNORMAL PULSATION

Normally the left ventricle contracts uniformly during systole. The left border moves in, the apex moves up and in, and the diaphragmatic border is elevated. The aorta and the pulmonary artery expand simultaneously (Fig. 1). Following myocardial infarction these movements may be altered in several ways. The most characteristic change, as we have stated, is a

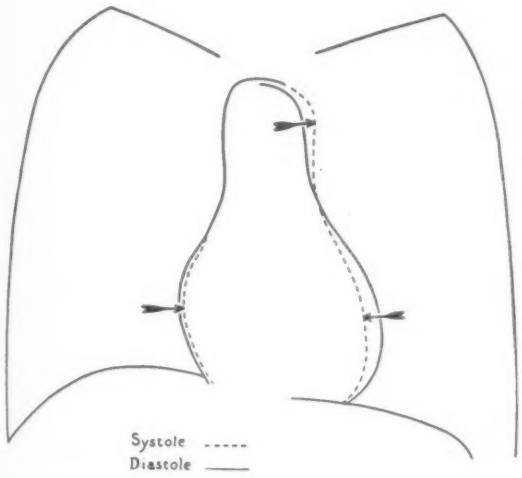

Fig. 1. H. L., female, aged nineteen. Normal heart showing normal ventricular pulsations.

localized systolic expansion or reversal of pulsation; as the normal portion of the ventricle moves in there is an outthrust of the area of infarction (Fig. 2), which expands simultaneously with the aorta. This results from the increased intraventricular pressure during systole, which causes the damaged muscle to give way, while the uninvolved portion contracts. Reversal of pulsation is often seen as a wave-like movement of the left ventricular border.

Occasionally the systolic expansion is incomplete and appears as a localized lag of pulsation; that is, the infarcted portion of the ventricle does not begin to contract until after the beginning of systole, when

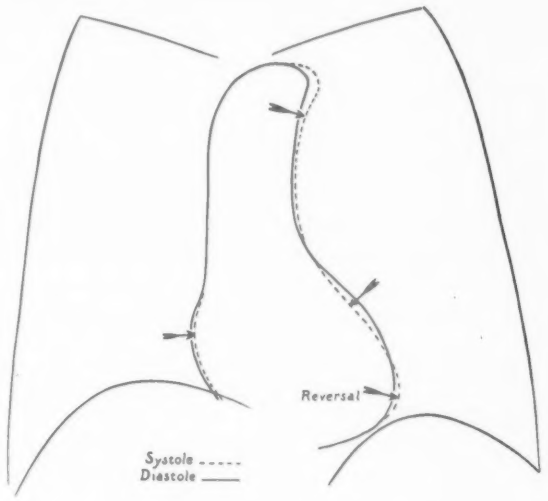

Fig. 2. M. F., male, aged fifty-five. Systolic expansion (reversal of pulsation) in coronary occlusion Attack in November, 1938; roentgenoscopic examination January, 1939.

the intraventricular pressure has fallen slightly.

Another variation of incomplete systolic expansion is "doubling" of pulsation. This appears to the examiner as a contraction, followed by a halt, and then another contraction. This phenomenon is difficult to explain. It seems that the infarcted muscle begins to contract early in systole while the intraventricular pressure is still below its maximum; as the pressure increases the

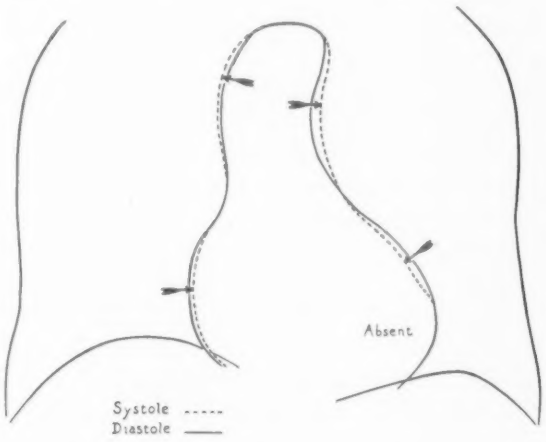

Fig. 3. I. S., male, aged forty-seven. Absence of pulsation in coronary occlusion. Attack in April, 1935; roentgenoscopic examination September, 1939.

muscle gives way, only to contract again later in systole as the pressure falls.

Less significant than systolic expansion or reversal of pulsation, but still definitely abnormal, is a localized absence of pulsation (Fig. 3), which may also occur in other types of heart disease. In myocardial infarction it represents an area of damaged muscle not powerful enough to contract in

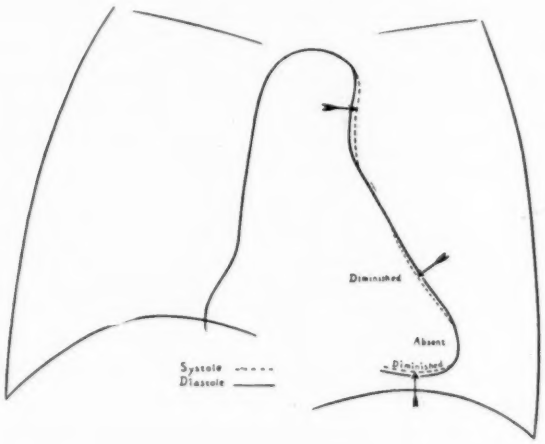

Fig. 4. H. G., male, aged fifty-five. Absence and diminution of pulsation in coronary occlusion. Attack in April, 1938; roentgenoscopic examination March, 1939.

systole, yet firm enough to withstand the rise in intraventricular pressure without expanding.

Finally, the infarcted area may produce merely a localized diminution in pulsation, with normal timing (Fig. 4).

Results in 300 Cases

Incidence of Abnormal Pulsation. Among the 164 cases of coronary occlusion, complete or partial systolic expansion or reversal of pulsation was observed in 70 (43 per cent) and diminution or absence of pulsation in 39 (24 per cent). Thus, ventricular contraction was abnormal in 67 per cent of the series. In the last 100 of the 164 cases, 53 per cent exhibited systolic expansion, and 21 per cent diminution or absence of pulsation, a total of 74 per cent with abnormal contraction. It is evident that reversal of pulsation, which probably occurs in over half the cases, is far more characteristic of myocardial infarction than either absence or diminution of pulsation.

Control Cases. In the 136 patients without coronary occlusion, who served as controls to determine whether the abnormalities described occurred in normal hearts or in other types of heart disease, the findings were as follows:

1. Normal hearts. Reversal or absence of pulsation was never observed in the 42 patients showing no evidence of cardiac involvement. The ventricular contractions appeared diminished in only one person.

2. Coronary disease (without occlusion). This group included 67 patients with clinical or electrocardiographic evidence of coronary sclerosis; hypertension was present in 26. In these patients, as in the normals, reversal or absence of pulsation was entirely lacking. However, localized diminution in contraction occurred 11 times.

3. Valvular heart disease. This group comprised 27 cases, including 15 with aortic insufficiency. Alterations in contraction were found in only 2 of the latter, as reversal of pulsation in one and diminution in the other.

Location of Abnormal Pulsation. In the 88 cases in which the site of abnormal pulsation was specifically noted, it occurred in the apical portion of the heart in 83 per cent. In 37 of these cases the apex alone was affected, in 33 the apex and supra-apical region, and in 3 the entire lower two-thirds of the left ventricular border. In 15 per cent, the abnormal pulsation appeared only in the middle third. Only twice was the upper third of the left ventricle involved. The area of abnormal pulsation tended to be the greater the larger the heart, involving one-half or more of the left border in some cases.

Site of Infarction and Incidence of Abnormal Pulsation. A study was made to ascertain whether the incidence of changes in contraction depended on the location of the infarct. The latter could be determined from the electrocardiogram in 141 cases

(Table 1). In 71 of these the electrocardiogram was of the Q_{1-4}, T_{1-4} type, indicating anterior infarction. In 49, the Q_3T_3 pattern of posterior infarction was present, and in 21 there was a combination of these patterns indicating infarction of both anterior

TABLE I
CORRELATION OF ABNORMAL VENTRICULAR PULSATION WITH SITE OF INFARCTION

Site of Infarction (Electrocardiogram)	No. of Cases	Abnormal Pulsation
Anterior	71	46 (65%)
Posterior	49	37 (75%)
Anteroposterior	21	15 (71%)
Normal electrocardiogram	18	9 (50%)

and posterior walls. Table 1 shows that whether the infarct was situated on the anterior or posterior surface of the left ventricle, or both, the incidence and location of abnormal pulsation were not influenced. The latter appeared in the posteroanterior view in approximately 70 per cent of the cases in each of the three groups. One might have expected that when the infarct involved the anterior surface of the left ventricle the abnormal pulsation would be seen best in the posteroanterior view, whereas a lesion on the posterior surface would appear only in the left oblique or left lateral position. Similarly, one would expect an infarct involving both surfaces to be seen equally well in both positions, and to be associated with a greater incidence of abnormal pulsations than an infarct localized to the anterior or posterior surface. That these assumptions are not borne out in this study may be attributed to the fact that the muscle bundles in the left ventricle are circular or spiral, and anchored at both base and apex. Hence an injury to a muscle anywhere in its course may destroy its leverage and weaken it throughout. As a result, abnormal pulsation is seen in the posteroanterior view even when the infarct is on the posterior surface.

Size of Heart and Abnormal Pulsations. Even in the presence of myocardial infarction the incidence of abnormal ventricular pulsation, particularly systolic expansion, was found to be related to the size of the heart. Thus, the heart was enlarged in 34 of the last 100 cases of coronary occlusion. Ninety per cent of these 34 cases exhibited abnormal contractions, and 79 per cent systolic expansion. Incidentally, there were 8 cases with ventricular aneurysm, all presenting large hearts and abnormal pulsations, reversal being observed in 7. On the other hand, only 66 per cent of the 57 normal-sized hearts disclosed abnormal pulsations, and only 41 per cent presented reversal. Furthermore, of the 9 remaining small hearts only 4 (44 per cent) revealed abnormal pulsations, and only 2 (22 per cent) systolic expansion. Hence, cardiac enlargement is an important factor in the production of reversal in coronary occlusion, although it is not essential since systolic expansion may appear in a small heart with myocardial infarction. It is interesting to note that systolic expansion was first observed by me in 1934, in a woman with a very small heart.[6] Although cardiac enlargement increases the incidence of systolic expansion, it will be shown that enlargement without myocardial infarction, as in hypertension, is not associated with reversal of pulsation.

Cardiac Pulsations in Hypertension. Hypertension alone is not a factor in the production of the roentgenoscopic abnormalities in coronary occlusion, since these were equally common in patients with and without hypertension. Thus, 40 of the last 100 patients studied had hypertension; 68 per cent of these presented abnormal pulsations, half of which were reversal. In the 60 non-hypertensive patients, abnormal contractions were present in 71 per cent, about half being reversal.

COMMENT

Diagnostic Significance of Abnormal Ventricular Pulsations. We have shown roentgenoscopically that localized abnormalities in pulsation of the left ventricle fall into three groups: (1) reversal of pulsation or

systolic expansion, (2) absence of pulsation, and (3) diminution. *Reversal of pulsation*, which is usually complete, or which may appear as a "lag" or "doubling," is always definitely abnormal, and may be considered pathognomonic of myocardial infarction. It was present in 53 per cent of our last 100 cases of coronary occlusion. The observation of systolic expansion should always arouse the suspicion of an old or recent myocardial infarction, and this will usually be corroborated by a careful re-examination of the patient's history and electrocardiogram. It is probable that a "lag" or "doubling" of ventricular contraction indicates a lesser degree of myocardial involvement than complete reversal or systolic expansion, but all these abnormalities were observed only in myocardial infarction. An exception to this rule has been noted in a few cases of aortic insufficiency with marked enlargement of the left ventricle, in which reversal was observed at the apex. It may be that when the left ventricle is markedly elongated contraction of the upper left ventricular segments precedes that of the apical region. There may also be a thinning of the apical region, despite the ventricular hypertrophy. On the other hand, hypertension and coronary sclerosis, no matter how big the heart, do not produce systolic expansion; if the latter is present, there has been an infarct. I may cite 4 cases in this series which were originally included in the group of coronary disease without occlusion. Three of these presented reversal of contraction, and one absence. When their clinical records were reviewed, a diagnosis of coronary occlusion was readily made in all four by analysis of the history and electrocardiograms.

Although not the essential factor, cardiac enlargement probably plays a rôle in producing systolic expansion, for this condition was more common in myocardial infarction when the heart was large. This is not surprising since a dilated heart presents, as a rule, a greater degree of coronary sclerosis and myocardial fibrosis; often coronary occlusion has occurred previously, and heart failure is more likely to set in. Consequently, when the acute infarction occurs, the function of the infarcted area is completely impaired, and may remain so for a considerable period. In a small heart, on the other hand, the loss of function is less severe, and contractility may return sooner. A corollary of this is the fact that the larger the area of abnormal pulsation the poorer is the prognosis. Thus, ventricular aneurysms are usually found in severely ill patients.

Absence or diminution of pulsation possesses less significance than reversal and must be interpreted with greater care. It has been observed that if the patient holds his breath under strain during roentgenoscopy, the contractions of the entire ventricle may disappear, although they never become reversed. Localized absence of pulsation, however, should always be considered abnormal, and at least suggestive of myocardial infarction. The loss of muscular power is of less extent than in reversal. Infarction may also be evidenced merely by localized diminution of contraction, but this, as well as absent pulsation, may occur in other types of heart disease, especially if the heart is enlarged and heart failure is present, for apical contraction is often impaired in a dilated heart.[1]

Interval between Onset of Coronary Occlusion and Roentgenoscopy. The opportunity to roentgenoscope a patient soon after an attack of coronary occlusion rarely occurs, but I have been able to observe abnormal pulsations in several patients one or two days after the attack. These were hyposensitive persons who came to the office unaware of being seriously ill. Changes in pulsation probably occur directly after the attack in most cases, and can be observed by roentgenoscopy. However, alterations in contraction have often been detected more than five years later. In this series the longest interval was fourteen and one-half years.

Prognostic Value of Abnormal Pulsations. In patients roentgenoscoped repeatedly over a period of months or years, the type

of abnormal pulsation has been seen to change. Occasionally it was possible to follow a systolic expansion (i.e., a complete reversal) through partial reversal, to absence or diminution of pulsation, and finally to normal pulsation, denoting a well healed scar. More commonly a complete reversal was replaced by a partial one, or by absence of pulsation. Such changes occurred chiefly in patients who had improved clinically; hence it appears that the type of abnormal pulsation may be of prognostic significance. Thus a change from reversal to absence or diminution of pulsation probably indicates some return of contractility in the involved area. However, distinct clinical improvement may take place despite a persistent localized systolic expansion. The roentgenoscopic findings are merely another aid in prognosis.

Value of Different views in Roentgenoscopy. For a time I suspected that abnormal pulsation when seen in the left oblique or lateral view indicated posterior infarction, but numerous exceptions have impaired this theory. The posteroanterior view alone, which permits the clearest visualization of abnormalities in contraction, may prove to be adequate for routine use. However, this can be determined only by further study. In small hearts one view is about as good as another; in fact, the left lateral position may sometimes be most helpful. This does not apply to patients with big hearts, or to those who are obese or have large breasts.

Aids in Roentgenoscopy. As a rule the roentgenoscopic detection of abnormalities in pulsation is simple if the procedure outlined is adhered to. Occasionally, however, some additional maneuvers must be employed: When the cardiac rate is very rapid, it may be necessary to exert pressure on the carotid sinus in order to slow the heart sufficiently for inspection of the ventricular pulsations. In very obese persons, the cardiac apex may be enveloped by a pericardial fat pad which obscures the ventricular pulsation. With a little care it is simple to distinguish the ventricular contour within the fat pad. Heavy breasts should be lifted aside if they obstruct a view of the cardiac pulsations. A high diaphragm in any condition may conceal the apex of the heart.

Reversal of pulsation may be simulated occasionally in normal persons by the fact that the contraction of the upper portion of the left ventricular border slightly precedes that of the apex. This may be even more evident in patients with mitral stenosis, in which the enlarged left auricle presents on the upper left cardiac border.

It is occasionally hard to visualize more than one segment of the left border simultaneously in order to obtain time relationships. This difficulty can be overcome by timing the pulsation of any part of the heart with the heart sounds; normally contraction is synchronous with the first sound.

Coronary Occlusion with Normal Electrocardiograms. In this series there were 18 cases of old infarction in which the electrocardiogram had returned to normal when the roentgenoscopic examination was made. Yet 9 of these actually presented systolic expansion! This emphasizes further the value of roentgenoscopy as a diagnostic aid in coronary occlusion.

SUMMARY

Roentgenoscopic observations of ventricular contraction in 300 private patients are recorded. More than half of these had coronary occlusion; the remainder included other types of heart disease and normal subjects.

The technique employed is described in detail. Roentgenoscopy is shown to be a simple and inexpensive method of diagnosing coronary occlusion with myocardial infarction.

Abnormalities in pulsation were present in 75 per cent of the cases of coronary occlusion. Systolic expansion (reversal of pulsation) of the left ventricle, observed in 50 per cent of these cases, is characteristic, if not pathognomonic of myocardial infarction. "Lag" and "doubling" of pulsa-

tion are incomplete forms of systolic expansion. Systolic expansion is seen in practically every case of large heart with ventricular aneurysm. Absence and diminution of pulsation were present in 25 per cent of cases with coronary occlusion, but also occurred in other types of heart disease.

The abnormal pulsations observed were located in the apical and the supra-apical portions of the left ventricle in almost 85 per cent of the cases studied.

The evidence of abnormal contraction did not depend on the location of the infarct as determined electrocardiographically.

The incidence of abnormal pulsation in coronary occlusion was found to be greater when the heart was enlarged. When the area of abnormal pulsation was large the prognosis was poor.

Systolic expansion may appear directly after the coronary occlusion and persist for many years. Its disappearance, or a change to absence or diminution of pulsation, is of favorable significance.

In normal hearts the pulsations are always normal. Hypertension alone does not produce changes. Disease of the coronary artery, without occlusion, did not exhibit systolic expansion or absence of pulsation. When these conditions are present, coronary occlusion should be suspected. Systolic expansion is occasionally seen in cases of aortic insufficiency with cardiac enlargement.

Roentgenoscopy should form part of the routine examination of every cardiac suspect. It may be positive when the physical examination and electrocardiogram are negative.

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ROENTGENOSCOPY OF THE PHARYNX IN MYASTHENIA GRAVIS BEFORE AND AFTER PROSTIGMINE INJECTION*

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DYSPHAGIA, usually accompanied by dysarthria, has long been known as one of the principal symptoms of myasthenia gravis. These two symptoms were first described by Goldflam[3] in 1893, and Boothby,[1,2] in 1932, regarding dysphagia as a serious sign, urged tube feeding to combat the difficulty in maintaining nutrition. As dysphagia indicates a disorder of the bulbar portion of the neuromuscular system, difficulty in swallowing is considered a dangerous sign, for it is often closely associated with dyspnea. Respiratory paralysis, moreover, is the usual cause of death in myasthenia gravis. We[5] have pointed out that dysphagia occurs in about 60 per cent of patients with myasthenia gravis and is the third most common symptom. It seems important, therefore, not only to recognize dysphagia when it is first encountered, but also to estimate how severely the pharyngeal muscles are involved. As it is well known that the pharyngeal muscles, either directly or through their myoneural junctions, are markedly affected in myasthenia gravis by prostigmine, advantage is taken of this fact to demonstrate the response to this drug by visualizing the pharyngeal cavity under the roentgenoscope during barium ingestion. Nineteen cases of myasthenia gravis have been so studied, along with a group of patients suffering from other forms of dysphagia, and the technique and clinical value of the procedure are outlined below.

TECHNIQUE

As the patient with dysphagia as a symptom of myasthenia gravis is often gravely ill, we have felt it advisable to have the patient remain over night in the hospital for the following test. In order to study the basic weakness of the muscles, all forms of treatment directed towards the alleviation of myasthenia gravis are removed twelve to twenty-four hours before the patient is examined. In severe cases this in itself may be a somewhat dangerous procedure if the patient has been taking large quantities of prostigmine bromide by mouth prior to the test. Under hospital conditions, however, with prostigmine methylsulfate readily available for intramuscular injection, should respiratory embarrassment or general collapse occur, one need not hesitate in removing the prostigmine or other forms of treatment. This does not offer any considerable problem in cases of mild myasthenia gravis and only needs to be considered in those cases with severe involvement of the pharyngeal and other muscles.

The patient is then examined through the usual fluoroscopic screen, either in a sitting or in a standing posture. The first examination determines the amount of diaphragmatic excursion and includes an inspection of the mediastinum for shadows indicating an increase in the thymic gland. At the same time inspection is made for calcification or masses in the neck or the pharyngeal region.

The patient is then given a swallow of a thin barium mixture and the way in which this mixture passes through the pharynx is observed. If the liquid barium is retained in the pharynx and in the pyriform sinuses in excessive amount and there is obvious difficulty in swallowing, a series of roentgenograms are taken before the injection of prostigmine. Prostigmine methylsulfate, prepared in advance so that it can be used

* From the Myasthenia Gravis Clinic, Massachusetts General Hospital, and with the cooperation of the Department of Roentgenology, Dr. George W. Holmes, Chief. Paper No. 9 in a series of studies on myasthenia gravis. The prostigmine was furnished by Hoffmann-LaRoche, Inc.

Fig. 1. Retention of barium in the pharynx in a patient with myasthenia gravis.

quickly in case of respiratory failure, is then injected intramuscularly in a dosage of 1.5 mg. (1/40 gr.) with 0.6 mg. (1/100 gr.) atropine sulfate. Prostigmine methylsulfate is ordinarily dispensed in 1 cc. ampules of 1–2,000 strength, each containing 0.5 mg. of prostigmine. It is therefore necessary to dissolve the atropine sulfate in the contents of 3 ampules. Recently a single ampule containing this amount of the drug has been made up, which is called a "diagnostic ampule" of prostigmine. It is now available for general use. Prostigmine is ineffective for this test if given by mouth. After fifteen minutes the test is again repeated with the thin barium mixture and the same observations are made as before the prostigmine injection.

In a severe case, before the injection of prostigmine, the thin barium will be retained in the pharynx in such a manner as to be obvious on the roentgenogram. Fifteen minutes later, in cases of myasthenia gravis only, the barium passes through the pharynx in a normal manner.

In patients with a lesser degree of pharyngeal weakness a thin barium mixture is not thick enough to be retained in the pharyngeal cavity. In such instances ordinary barium paste is used, only slightly diluted (Figs. 1 and 2). It is unwise, however, to use thick paste on the first examination. Patients may retain this mixture to such a degree that respiration is embarrassed and death may take place. It should be emphasized, therefore, that if retention is shown by the thin barium mixture, there is no indication to try a thicker barium paste. To evaluate the results the same mixture of barium should be used before and after the prostigmine injection.

CLINICAL IMPLICATIONS

The degree of improvement in swallowing as demonstrated by this method is an excellent adjunct to the "prostigmine test" already described by us[4] for the diagnosis of myasthenia gravis. We used the same amount of prostigmine and made our obser-

Fig. 2. The same patient fifteen minutes after an intramuscular injection of prostigmine.

vations on the external manifestations of the disease, such, for instance, as ptosis, diplopia, loss of facial expression, and general weakness. Roentgenoscopic examination of the pharynx, therefore, is another form of the "prostigmine test." It only shows, however, the condition of the patient at the time of the examination and does not give a complete indication of the extent, severity, or prognosis of the disease. Patients with myasthenia gravis have remarkable remissions and relapses and changes may occur within a few weeks. It is not unknown to see a patient with marked dysphagia and with extensive retention of barium in the pharynx, recover within a few weeks, so that the swallowing reflex is practically normal and all the barium is removed from the pharynx without the aid of a drug such as prostigmine. Of the 19 cases examined by this method, however, 17 patients responded so strikingly to prostigmine by injection that practically no barium was retained in the pharynx. These same patients had also done well under prostigmine treatment by mouth.

Dysphagia due to other causes, such as progressive bulbar palsy, does not respond to the test.

CONCLUSIONS

The observation of the swallowing reflex in patients with dysphagia due to myasthenia gravis, by barium ingestion, is a simple and valuable form of the "prostigmine test." Barium is quickly swallowed after the proper amount of prostigmine is injected in cases of myasthenia gravis; improvement does not occur in other diseases. The technique of roentgenoscopic examination and the clinical implications of the test are discussed.

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ROENTGEN FINDINGS IN THE EXPLORATION OF THE BILE DUCTS*

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IN DISEASES of the gallbladder and bile ducts roentgen diagnosis is of clinical value only in the exploration of the gallbladder (cholecystography) while in examination of the bile ducts it is of practically no value.

On the other hand, we know the frequency and clinical importance of the complications of these diseases, which react chiefly on the excretory bile ducts, making their diagnosis, prognosis and treatment more difficult.

The impossibility of visualizing the bile ducts and the clinical importance of studying the bile tract suggested to experimenters the possibility of making an examination through the fistulas which are so frequently created surgically. Cotte, in 1925, presented some experiments in "exploration of the bile ducts with lipiodol in cases of fistula," asserting that the exploration of the bile ducts with lipiodol is absolutely harmless and capable of giving the most valuable roentgen data.

Berard and Mallet Guy, surgeons of the Lyon school, hold that cholangiography is the most valuable method of examination in the study of diseases of the bile ducts. An extensive study has been made of the functional and anatomical interpretation of the different roentgen appearances to such an extent that, based largely on the data collected in these cholangiographic studies, the surgical indications for cholecystectomy and cholecystostomy have been defined, showing that the latter operation is the method of choice in the majority of lesions of the bile ducts. We see therefore that the progress attained by this method has originated from the first investigations, in which a simple fistulography, made from curiosity was only an isolated test without any clinical value.

From that time up to the present, this method of roentgen examination has extended and been adopted in all countries, but sometimes so slowly and with so little enthusiasm that it might be thought that the method was of little value. For our part, since 1923 we have been making these roentgen examinations in the Radiological Institute of Buenos Aires and have found that they are absolutely harmless; in the beginning we used iodized oil which at first satisfied us as being a contrast substance of good opacity and harmless, but soon we saw that its density and immiscibility did not result in good anatomical and functional observation of the bile ducts. In 1930 (?) we began to use the solutions of thorium which we found was the ideal contrast medium as it combined the three necessary qualities, namely, opacity, harmlessness and miscibility.

In 1933 at the first American Congress of Radiology in Chicago I had the honor of reading an article on the first experiments made with solutions of thorium and called attention to the clinical importance of the functional and anatomical data obtained with these aqueous solutions on the fluorescent screen and on roentgenograms. From that time up to date we have made this roentgen examination of the bile ducts (cholangiography) in 518 cases of diseases of the bile tracts (lithiasis, various forms of cholecystitis, obstructions of the bile ducts from different causes, abnormalities in the flow of bile, etc.). We have been able to gather many data and roentgen observations which we consider of great functional and clinical importance to which the spe-

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cialists and surgeons of the Rivadavia Hospital of Buenos Aires have given special attention; it is now a common clinico-surgical method in diseases of the bile ducts and a number of articles have been published on the subject.

This exploration of the bile ducts may be made during operation (cholangiography during operation), as Mirizzi of Argentina recommended in his book published in 1933 "Cholecystectomy without Drainage," or after having first established an operative biliary fistula (cholangiography after operation). For our part we perform only postoperative cholangiography, because we attribute great value to the minute roentgenoscopic and roentgenographic examination which in our opinion would enormously complicate the surgical operation, with detriment to both the roentgen observation and the operative result.

TECHNIQUE

Once the operative fistula has been made either through the gallbladder or the common duct and as soon as the condition of the patient permits it (after three or four days), the opaque fluid (thorotrast Heyden, pure or 50 per cent, heated to body temperature) is introduced under roentgenoscopic observation. The liquid is simply poured in if there is only a functional change in the sphincters, or injected with a syringe under slight pressure if there is an obstacle to its entrance. The amount to be injected varies, depending on the condition of the ducts, generally 30 to 50 cc. It is absolutely harmless. There is no fixation of thorium in the epithelial tissue.

None of the criticisms that have been made of the method have any value whatever.

When the operative fistula is made through the gallbladder the functional and anatomical data are more accurate, because the filling of the ducts takes place from without inward and there is no greater trauma than there is in drainage of the common duct.

The patient, placed on the roentgen table, is first given an amount of liquid which varies from 10 to 20 cc., depending on the size of the gallbladder, in cases of fistula of the gallbladder and common duct or drainage of the duct. Observation is made under the screen of the filling and capacity of the gallbladder and all possible anatomical and functional findings are recorded.

FUNDAMENTALS OF AND INDICATIONS FOR CHOLANGIOGRAPHY

The pathology of the gallbladder and bile ducts at present constitutes an important part of clinical surgery which should not be neglected. Any observer who frequently has occasion to observe this class of patients will see that mistakes and surgical complications are perhaps more frequent than in any other disease.

An over-simplified clinical-surgical conception of these cases has been shown to have serious consequences.

We have had an opportunity in the Radiological Institute of the Rivadavia Hospital (Women's Hospital) to follow up these observations in a large number of cases and control the observations of Doctors Bengolea, Zabala, Del Pino, Velazco Suarez and Masciotra, always made with extreme care before and after operation and whose conclusions are on the whole those which we give here. The object of postoperative cholangiography is to study the morphological and functional appearance of the bile ducts.

The chief organic or anatomical factors which can be cited as causes of the different lesions which contribute to forming the varied clinical picture of affections of the liver and bile tract will be given only in a general way.

(1) *Gallbladder.* Presence of calculi, number, quality and quantity. Condition of the gallbladder, size, content, appearance and constitution; appearance of its walls, adhesions, obstruction of and changes in the sphincter (calculi or tumor).

(2) *Excretory Bile Ducts.* Calculi inside it, large or small, site and distribution, number, appearance, fixation, alterations

FIG. 1. Postoperative stenosis of the third portion of the common duct. *1*, the common duct above the partial stenosis; *2*, the rest of the common duct from below the stenosis; *3*, the duodenum. Dilatation of all the biliary tree. The duct of Wirsung is clearly visible.

of the ducts from internal or external obstruction, calculous, tumoral, or inflammatory; or concomitant partial or total dilatations.

(3) *Peritoneum and Adjacent Organs.* Pericholecystitis, periduodenitis, various local peritonitides, infiltration of the hilum and vicinity, adenitis, hydatid cyst or malignant tumors, perforated ulcer of the stomach and duodenum, diverticula and diverticulosis of the duodenum.

(4) *Lesions of the Pancreas.* These are not very well understood and clinico-roentgenological observation of them is difficult. They include acute, subacute and chronic pancreatitis, lithiasis of the pancreas, simple and hydatid cysts.

Functional factors also produce a varied physiopathological picture. These have been known for a long time but recently their existence and interpretation have been better controlled by cholangiography.

We think that the time of experimentation has been to short and the number of investigators too small to establish definite data of accurate diagnostic value in the various lesions, and for my part I merely wish to present to you the most striking clinico-roentgenological findings seen on the fluoroscopic screen and on films, as it is a question of establishing one single undoubted fact, that is, *the clinical importance of this new method of roentgen examination.*

It should be carried out in any complication of disease of the bile tract and whenever we suspect any anatomical or functional change in this system, the clinical diagnosis of which we wish to establish definitely. For our part we think that in a large number of cases surgical operation in diseases of the bile tract should be performed in two stages, the first a simple operation for draining the bile tract, and establishing in this way a biliary fistula, and then a roentgen examination for determining the type of the final operation which is carried out as the second stage.

We believe also that postoperative cho-

FIG. 2. *1*, pronounced widening of the final portion of the common duct produced by Kehr's tube; *2*, the duct of Wirsung clearly visible and enlarged; *3*, the remainder of the thorotrast in the bottom of the stomach.

langiography will limit the practice of duodenostomy.

This is the method which the majority of the surgeons in the Rivadavia Hospital in Buenos Aires seem to have adopted in the greater number of cases.

ROENTGEN FINDINGS IN THE NORMAL GALLBLADDER

Generally the gallbladder can be filled very easily through its fistula and we can observe the actual existence of the cholecystic sphincter already described by physiologists and experimenters. The solution is stopped at this level for a few minutes, showing a regular and blunt sphincter which soon yields to the contractions of the gallbladder, which become more accentuated and regular. They are painless and involuntary and sometimes very hard to observe.

The gallbladder empties in stages, that is to say its contents is evacuated little by little; the emptying time, according to data which are in agreement with other physiological and roentgen observations (Boyden's test) is about fifteen to twenty minutes.

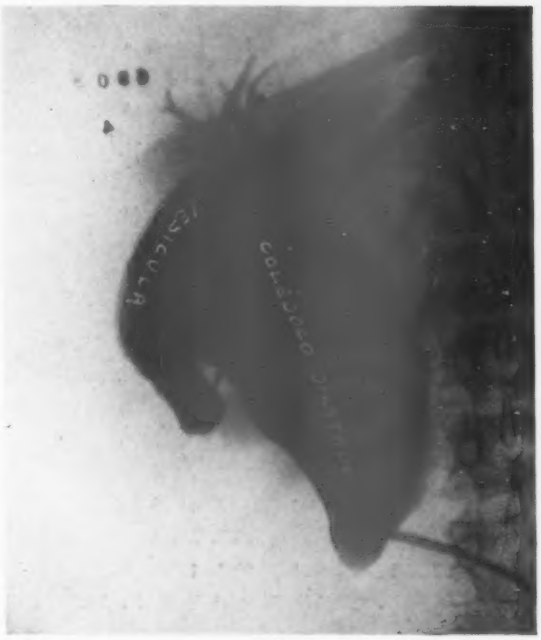

Fig. 4. Enormous congenital dilatation of the common duct; the sphincter of Oddi impermeable. No stones observed nor pathological stenosis of the organ, but the thorotrast did not pass. The rest of the hepatic channels somewhat dilated. The gallbladder lengthened without apparent deformity.

Fig. 3. *1*, common duct very much enlarged with several stones overlapping at the end; *2*, gallbladder; *3*, intrahepatic channels of the left lobe of the liver.

Once the cholecystic sphincter is overcome the liquid rapidly fills the cystic duct and then immediately the common duct and sometimes the hepatic, after which it is detained again near the opening of the duodenum or at Oddi's sphincter which generally remains closed to the passage of the liquid for a time somewhat longer than that at the cystic duct; slow and regular peristaltic waves can be seen which often dilate the sphincteric portion of the common duct in the form of a drumstick, until the contraction of the sphincter is overcome and the liquid begins to fall into the second vertical part of the duodenum, slowly and regularly.

The hepatic is harder to fill than the common duct. If the rapidity of the entrance of the opaque liquid is increased a little a better visualization of the hepato-common duct is obtained; this maneuver changes the

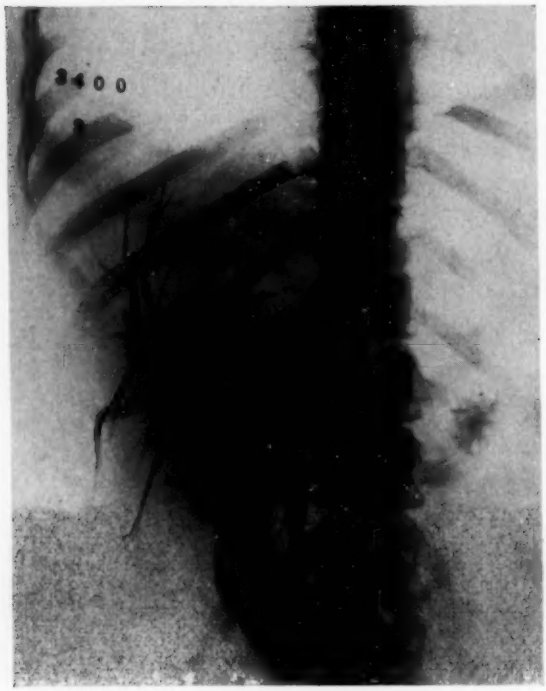

FIG. 5. The pancreatic portion of the common duct is permanently altered. Partial stenosis of the channel. No stones. Partial stenosis of the common duct because of stenosing pancreatitis.

functional condition of the sphincters, so that it should not be practiced until after the functional observation, which we think is very important, has been completed. The cystic duct always appears sinuous or in the shape of a spiral, and its opacity often persists in spite of the fact that the common duct has begun to empty, as if there were a cystic dilatation which is to be considered normal. Its valves are not visible on roentgen observation.

The common duct is more visible than the cystic on the screen, due to the greater amount of contrast substance required to fill it; it has regular walls and is 5 to 6 cm. in diameter. In order to render it more visible the pressure of the liquid should be increased, until slight pain is felt, on which the pressure should be stopped.

The ampulla of Vater can be seen in some cases as a small sessile shadow attached laterally to the shadow of the duodenum and forming a part of it. According to our experience its visualization should be considered a pathological condition of the ampulla.

Roentgenologically the sphincter of Oddi should be considered as such, for it always shows all the functional and morphological characteristics of true sphincters. That is to say that liquids injected are detained at this level of the common duct, appearing normally as a tube with a cul-de-sac, with regular, more or less rectilinear walls which undergo changes in form of peristalsis. Moreover a small sphincteric canal is often observed roentgenologically, or at other times an absence of shadow between the common duct and the duodenum which corresponds to the contraction of the sphincter itself. On the other hand, there are pathological anatomical or functional changes of the sphincter which produce changes of the normal shadow similar to those observed in the other sphincters as we shall see farther on. It has not been pos-

FIG. 6. Twenty days later, cholangiography revealed a number of large stones lodged in the common and other intrahepatic ducts. No obstruction of the sphincter of Oddi. The same afternoon the patient eliminated six stones. A roentgenogram with thorotrast still revealed the presence of several stones as well as the dilatation of the biliary ducts.

sible in our observations so far to make an accurate differentiation between the superior or antral sphincter, innervated by the vagus, and the inferior or papillary, innervated by the sympathetic, the study of which deserves special attention just now, because of its importance in the clinical conception of the dyskinesias.

We think that for the present the bile tract should not be considered a simple inert system of conduction but as an active and regulable system, which has an exquisite systematized function which is under the control of the vegetative nervous system.

ROENTGEN FINDINGS IN THE PATHOLOGICAL GALLBLADDER

In order to simplify and classify this study this section will be divided into three parts: (1) roentgen findings in biliary lithiasis (gallbladder and bile ducts); (2) roentgen findings in functional changes in the bile ducts; (3) roentgen findings in other lesions of the bile tract and adjacent tissues.

Roentgen Findings in Biliary Lithiasis. The roentgen findings in lithiasis of the gallbladder have almost all been determined by cholecystography, the diagnostic value of which is well known and the place which it occupies in the clinical examination of the organ.

On the other hand, one of its most frequent and serious complications, that is lithiasis of the hepato-common duct, escapes direct roentgen diagnosis or the cholecystographic test almost completely. Moreover, the clinical development and progress of these complications may take place slowly, except in rare cases in which the obstruction may be acute, and its symptomatic manifestation is generally confused and varied, depending on the functional and organic changes which it produces on the excretory ducts.

The usual seriousness of these hepatocommon duct complications perhaps requires the greater part of the time devoted to cholangiography. The surgical treatment of the cases suspected of obstruction of the ducts has been hastened by establishing the operative indications early, which greatly improves the operative prognosis of obstructions of the common duct and encourages early cholangiographic exploration.

Moreover, this practice makes it possible to give other medical treatment of lithiasis at the opportune time, especially the direct lavage of the bile ducts with paraffined ether and Prinban's test; this method established some years ago in the Rivadavia Hospital of Buenos Aires has given great satisfaction to the surgeons, greatly improving the statistics in the cases treated. The roentgen appearance of the shadows of calculi in the ducts after opaque filling is similar to that obtained in gallbladder calculi with the Graham-Cole test, that is to say they are negative shadows rendered manifest by the contrast fluid. Therefore the necessity for using aqueous opaque solutions, the slight density and good miscibility of which make this method of roentgen examination an irreplaceable method in clinical observation, whose characteristics are not to be confused with those of other conditions.

The introduction of air with the liquid during the injection should be avoided as we have mentioned before, because by the observer with little experience its shadow might be confused with that of non-existent stones; but calculi always keep the triangular or polyhedral form of the sloping surface of the stones. The image does not vary in the different stages of the manipulation and generally it does not change in size or position. The presence of two or more shadows, however, favors the diagnosis of calculus of the ducts. If there is any doubt the interpretation of the different films of a series will remove the error. When there is a calculous obstruction of the neck of the gallbladder or the cystic duct in cases of gallbladder fistula, the distention of the gallbladder is painful. The use of aqueous solutions permits of better visualization of the shadow of the calculus because it is easier for these solutions to penetrate between the walls of the duct and the calcu-

lus. Therefore almost always the roentgen images when aqueous solutions are used are lacunar images, not to be confused with others, that is to say they take the appearance of a stirrup shadow, as we call it. They are also known as "cul-de-sac" shadows.

When the liquid does not succeed in penetrating between the wall and the calculus, the terminal shadow of the common duct is in the form of a half-moon with the horns downward, and it is generally accentuated when the calculus totally obstructs the sphincter of the duodenum.

When these multiple calculi are small the image is that of a honey-comb and the calculi always seem to be agglomerated in the terminal part of the duct.

The site of the obstruction of the cystic duct may be in the vesicular or canalicular portion. In the former case the cystic duct will be invisible but there will be a semilunar or lacunar calculous shadow. When the calculus is in the duct we will see a part of the proximal portion of the duct and the calculus inside it. In these cases the introduction of the opaque liquid produces pain on distention with 10 or 15 cc., depending on the size of the gallbladder. These obstructions from residual calculosis are few in number but they are sometimes seen. We should not forget the precarious conditions in which these patients sometimes have to be operated on.

Sometimes we have seen a shadow of a calculus in the gallbladder itself after it has been emptied surgically.

The calculous shadows in the cystic duct may be small and numerous or large and solitary. The gallbladder, the function of which is inhibited by calculus of the cystic duct, is generally large and full of liquid but it may be small and contracted and full of calculi.

The most frequent site of duct calculi is without doubt the common duct. Calculi of the common duct may be solitary or multiple. They may be located in different parts of the duct but usually in the terminal part; they are sometimes free and sometimes fixed to the walls of the common duct, producing partial or total obstruction. As a natural result, these obstructions cause greater or lesser dilatations of the duct which may reach enormous size similar to that of the small intestine.

We find that sometimes a large calculus does not cause total obstruction while a smaller one obliterates the canal. This is because obstruction depends on the shape of the calculus which may be facetted and irregular and leave part of one of the walls free so as to permit the passage of small amounts of bile or opaque solution.

The dilatations of the common duct may be accompanied by an increase of peristalsis with probable antiperistalsis, or generally decrease or absence of peristalsis, as is frequently seen in old chronic obstructions at the sphincter of Oddi. In these cases the common duct looks roentgenologically like a very much dilated inert canal receiving a large amount of contrast fluid.

Its anatomical position immediately above and inward from the duodenum and its characteristic appearance make it impossible to confuse it with the image of any other organ. Calculi in the sphincter of Oddi may permit of the passage of a small amount of opaque liquid, sufficient to show immediately after the negative shadow characteristic of calculus a small visible sphincteric canal. On the other hand, when the calculus is located in the ampulla of Vater, this roentgen image of the canal disappears and the shadow of the calculus becomes a part of the shadow of the duodenum. We believe this diagnosis of the true position of the calculus is very important as it may indicate the proper path of approach for extracting it, through the common duct in the former case and through the duodenum in the latter.

In addition to this direct observation of the calculi, there are accessory signs which may also accompany lithiasis of the common duct. The most important is dilatation of the extrahepatic ducts from chronic biliary distention.

As soon as the cause of the obstruction is

eliminated the dilatation of ducts decreases little by little but we have never seen during the time the drainage remains a total restoration to normal diameter. Just as frequently a small dilatation of the duct persists due probably to atony of the duct or a certain inflammatory or contractile condition of the sphincter, particularly in cases of calculous obstruction of the sphincter.

The anatomical condition of the common duct should be taken into account before withdrawing drainage permanently.

Calculi are much less frequently located in the hepatic duct and in the intrahepatic ducts of the second and third order. Almost always they produce partial or total obstruction, are fixed and are accompanied by different degrees of dilatation of the high bile ducts. Generally they are accompanied by multiple calculi of the common duct. Except for the calculi located in these upper ducts, intrahepatic lithiasis is rare. We have seen only one case, accompanied by multiple lithiasis of the hepato-common duct.

Another accessory sign of lithiasis of the sphincter is visualization of Wirsung's pancreatic duct, but this is not exclusive, as it is seen also in all partial or total obstructions of the common duct at the sphincter. The latter appears as an opaque canalicular shadow of much smaller diameter than the normal common duct and which originates inward from it, near Vater's ampulla, projected over the duodenal shadow and then directed upward and inward and continued in a more or less undulating form parallel to the greater curvature of the stomach. Its filling does not produce any immediate reaction or complication, and only during the injection the patient sometimes complains of slight pain in the epigastrium.

In its beginning part it forms with the common duct a V open upward, which is generally visible for only 4 or 5 cm., and it may be more or less dilated, but usually does not reach any very great size. We have seen 2 cases of obstruction of the papilla, one by lithiasis and one by stenotic pancreatitis in which it was possible to see the whole of the canal and even its secondary and tertiary branches without producing any immediate or secondary consequences.

We believe that the use of aqueous solutions is the only possible way of producing this finding, which we are the first observers to describe, according to medical literature. We have seen it in cases of lithiasis of Vater's ampulla with partial or total obstruction, in stenotic pancreatitis or tumors of the papilla and also in functional changes in the sphincter of Oddi and in biliary dyskinesia. As to the interpretation of filling of Wirsung's duct, we believe it should always be considered an abnormal functional or anatomical condition, but up to the present time we cannot give a definite interpretation. In cases of calculous obstruction above Oddi's sphincter it is rare to see partial or total filling of the pancreatic duct, which we consider an important sign of diagnostic value in differentiation between lesions of the sphincter and lesions of the papilla, and in indicating the route of operation in obstruction and drainage of the common duct or duodenum.

In cases of obstructive odditis Wirsung's duct also is visible, but the differentiating roentgen signs described are very evident in these cases.

In the hepatobiliary dyskinesias with functional changes in Oddi's sphincter, we have also seen it fill, but the filling is much less pronounced than in the cases previously described. Taking into account these roentgen findings and the characteristic appearance of the sphincter and the sphincteric canal, it is possible to make a differential diagnosis between the two lesions as we shall see in the following discussion of the hepatobiliary dyskinesias.

In our opinion any calculous obstruction of the common duct verified or suspected during operation should be submitted to this cholangiographic examination after having merely established a gallbladder fistula in the first stage and leaving for a varying length of time the performance of the final operation, according to data collected on clinical and roentgen examination. With this preliminary operation a con-

dition of drainage is established that is very simple and favorable for the patient, and avoids the inconveniences of drainage of the common duct for the purposes of future roentgen examination. It is for all these reasons that we believe, as a general rule, in the evident superiority of postoperative cholangiography, as compared with that performed during the operation itself, which would be ideal if the multiplicity of the hepatobiliary lesions would permit of easy and simple roentgen examination, which is never the case even for experienced observers.

We do not wish to insist on the well-known fact of the difficulty of manual or instrumental exploration of the bile ducts for determining the presence or absence of an obstructive calculous lesion. From what we have seen at close range in a great num ber of these clinical cases of the series of difficulties in being able to determine the absolute permeability of the bile ducts during operation and the undoubted usefulness of this roentgen exploration, we shall always remain faithful defenders of this method which we do not doubt will in the near future be a common method of exploration in the anatomical and functional examination of the bile tract.

Hepatobiliary Dyskinesias. The extrahepatic bile system may, for anatomico-physiological and clinical reasons, be considered as divided into two parts for special consideration, which will make it easier for us henceforth to give a description of the different roentgen signs which we are studying in this chapter on the biliary dyskinesias: (1) the concentrating system and (2) the conducting system.

(1) In the roentgen observation of the first system we shall take into account the functional and anatomical changes which occur in the gallbladder, the cholecystic sphincter (Lutkens) and in the sphincter of the common duct (Oddi).

(2) In the conducting system we should study the flow of bile from the hepatic gland to the gallbladder, from the latter to the duodenum and finally that from the liver to the duodenum, which takes place through the bile ducts, the active function of which seems to be regulated by appropriate mechanical and reflex factors, with rhythmical intervention of the gallbladder and common duct sphincters, under the control of the sympathetic and parasympathetic nervous systems.

The anatomical and functional changes in these factors produce essential changes in the normal functioning of the bile, which cause dilatations of the ducts, for which reason they are of such great importance in the production of calculi and in the painful hepatobiliary syndrome.

The studies of Westphal, Lutkens, Berard and Mallet Guy, and many others, have brought out a number of useful data in the possible interpretation of this important subject, the determination of which is not, however, at all clear or final.

The control of all these experimental observations will enable us, thanks to roentgen exploration of the bile system, to establish their true physiopathological value.

We have made this roentgen observation in 68 cases of non-calculous cholecystitis, studying by means of operative drainage of the gallbladder the functional and anatomical condition of the bile ducts.

In all of these preliminary cholecystotomy was performed with the least traumatism possible, taking great care also in all the details of technique of cholangiography in order to respect bile function as much as possible. The data collected with the use of an aqueous solution as a contrast medium have protected us from many doubts and errors noted by other authors who have evaluated the roentgen findings made with oily solutions, which we consider absolutely unsuitable. The picture of the dyskinesias is very obscure and it may be said that it corresponds to the present conception of the painful pseudo-lithiasic gallbladder syndrome, in which it is known that cholecystectomy does not give the best therapeutic results. Therefore the importance of recognizing the true physiopathologic concondition of the bile tract, the changes in

which, hard to observe, persist or increase after the development of the conditions created by an operation which is frequently unsuitable or even contraindicated. It is necessary in these examinations to change the normal function as little as possible. This is accomplished by putting the patient at rest on suitable diet for forty-eight hours before the examination and then taking great care in the technique of cholangiography according to the indications already described.

In chronic cholecystitis without stone, in which the picture of infection is the exception, the gallbladder is frequently seen small in size on the fluoroscopic screen; it is hyperperistaltic and the cholecystic sphincter contractile, arresting the passage of the opaque fluid for some minutes. Exaggerated distention of the gallbladder which is brought about by 8 to 10 cc. is painful. The cystic duct is generally contractile and continuously visible, while the hepato-common duct appears somewhat dilated and with hyperperistalsis. The contractions of the common duct are clearly visible and sometimes there is antiperistalsis. There is also a condition of transitory contraction of Oddi's sphincter. It is at this level that the condition of spasmodic contraction of the whole bile tract is most evident and real, being accompanied by a distention of all the bile tract, but particularly marked in the hepato-common duct. This biliary distention is accompanied by slight dilatation of the hepatic and common ducts generally with hyperperistalsis, varying according to the degree of the lesion. The canal of the intrapancreatic sphincter appears pointed roentgenoscopically, conical and with regular borders, as in the cases of chronic stenotic pancreatitis, but much less pronounced and without the persistence which appears in those cases and which we have already described.

Moreover the hyperperistalsis of the duct is more pronounced than in those cases; the persistence of these characteristics in a series of roentgenograms is a sign of organic lesion. Moreover, antispasmodics have a sedative action on the sphincter while opiates tend to have the opposite effect, which we believe can be used clinically as a sign of diagnostic value.

An increase in the pressure of the opaque fluid which fills the common duct through the gallbladder fistula produces pain, while in cases of chronic pancreatitis it is easier to make all the bile tract visible without causing this distention pain.

We may therefore conclude that functional distention is more transitory than organic and that the irritative condition of the neurovegetative system produces a roentgen picture which can be differentiated from that caused by the organic obstructions which we shall now consider.

Findings in Organic Non-calculous Obstructions. The precision of roentgen observation may give useful data. We have just described the appearance of the image in the dyskinesias; now we will describe the findings observed in other obstructive, non-calculous lesions.

Before mentioning the roentgen signs frequently observed, we wish to state that it is necessary to make a very minute study, collecting a very numerous series of images of the sphincter which will enable us to obtain precise details.

In retractile odditis (Del Valle, Buenos Aires) and in spasmodic odditis the common duct is very little dilated, though there is biliary distention. The intrahepatic duct is very short and slightly conical, with regular walls and without the undulations seen in cases of stenotic pancreatitis. After it has reached the terminal part of the sphincteric cone the opaque liquid is seen to be detained without any great irregularity of its shadow, and then to fall little by little into the duodenum, after a more or less persistent detention. Between the slight shadow of the duodenum and the sphincter a clear space is frequently observed which corresponds to the site of the lesion. There is no deflection or deviation of the sphincteric canal.

The differential roentgen diagnosis of these lesions is difficult and we think that

the one should be considered the result of the other, following a prolonged period of continuous irritation of the sphincter and of secondary biliary distention with the concomitant chemical change in the bile. We cannot say what is the effect of antispasmodics on the changes in the sphincteric shadow which we are now studying.

We have observed Wirsung's duct more frequently in retractile odditis, and consider it a probable differential sign.

In cancer of the head of the pancreas, obstruction of the common duct is one of the first manifestations of the disease. The condition of the patient is generally excellent and the only clinical alarm signal is the persistent icterus.

We have observed that the roentgen image is characteristic from the beginning.

The common duct appears dilated but without reaching the size seen in calculous obstructions. In the terminal part, instead of ending in a cone as in inflammatory pancreatic lesions, the lumen decreasing to the sphincter, it ends abruptly and with a convex border, without deflection and with peristalsis much decreased or absent. Between the terminal part of the common duct and the duodenum, a fact apparent by the gastric route, there is an absence of shadow for 1 to 2 fingerbreadths, which corresponds to the site of the pancreatic tumor. There are no vestiges of the pancreatic sphincter. Wirsung's duct is invisible.

In cases of *carcinoma of Vater's papilla* the roentgen image was very similar. The common duct was moderately dilated and the shadow of the sphincteric canal was irregular and its central canal deviated to one side at the site of the intracanicular tumor; there was partial obstruction, the opaque fluid passing into the duodenum with great difficulty. The pancreatic duct was visible in some cases and in others not visible.

It can be seen from the description just given that there are important roentgen signs which enable us to suspect the causal diagnosis of chronic obstructions of the common duct, the study of which we believe is of great enough clinical value to prove the importance of postoperative cholangiography using aqueous opaque solutions.

Vol. 45, No. 3

ANEURYSM OF THE LEFT VENTRICLE*

A REPORT OF TWO CASES

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ANEURYSMS of the heart are rarely diagnosed in vivo. They probably occur more frequently than the literature indicates, for the diagnostic criteria of the chronic form are not characteristic unless there is a definite deformity of the cardiac outline. The electrocardiographic findings are not definitely diagnostic and the symptoms are those commonly seen in late coronary disease and progressive heart failure.

The first case of aneurysm of the left ventricle subsequent to coronary sclerosis, diagnosed roentgenologically, was reported by Sézary and Alibert[11] in 1922. In 1927, Lenk[8] reported a case but did not have postmortem confirmation of the diagnosis. Steel,[15] quoting Pletnew,[10] states that in 300 reported cases only 6 had been diagnosed antemortem. Pletnew added the seventh and eighth but did not show roentgenograms. Fogel[7] reported a case in a living patient, and Sigler and Schneider[14] reported 3 cases diagnosed in vivo and confirmed at necropsy. Schwedel and Gross[12] present a roentgenographic and postmortem survey of the literature showing roentgenograms of one case. In the 6 cases reported by Steel, none were diagnosed antemortem and postmortem confirmation was obtained in one. There are reported here 2 cases of aneurysm of the left ventricle in syphilitic individuals diagnosed roentgenographically and observed over a period of three and four years respectively with confirmation of the diagnosis at necropsy.

PATHOLOGY

Ventricular aneurysms may be acute or chronic. The acute are formed by infected emboli lodging in the coronaries to produce abscesses with bulging and rupture. These usually terminate in instantaneous or sudden death. Others show myocardial failure weeks or months after an abrupt or stormy upset with critical developments and physical signs of coronary occlusion. These generally terminate suddenly within a few hours or days. Still others have an abrupt onset with clinical findings of coronary disease that recover and survive with a crippled myocardial efficiency. This chronic form is more common.

Rapid large arterial occlusions produce sudden or instantaneous death. When the occlusion is very slow, there is capillary expansion and compensation with the formation of infarcts either with or without bulging of the cardiac contours. Observers are agreed that chronic cardiac aneurysms are produced by a gradual narrowing of the lumen of the coronary vessel by arteriosclerotic changes with a final occlusion by a thrombus. The rate of occlusion must be too slow to produce sudden death and too rapid to permit capillary expansion and compensation. The size of the vessel involved and the state of the myocardium are important factors in the production of ventricular aneurysms. Chronic aneurysms rarely rupture but terminate by a progressive myocardial failure. The anterior descending branch of the left coronary is most frequently affected[16] and infarcts develop in the anterior wall of the left ventricle and interventricular septum.

The restriction of the blood supply by the occlusion of the artery gives rise to an anemic necrosis and an acute myocardial softening. This yields to pressure and undergoes a fibrous tissue transformation leaving the heart wall thin. These scars are usually single but may be multiple.[12] Clots form

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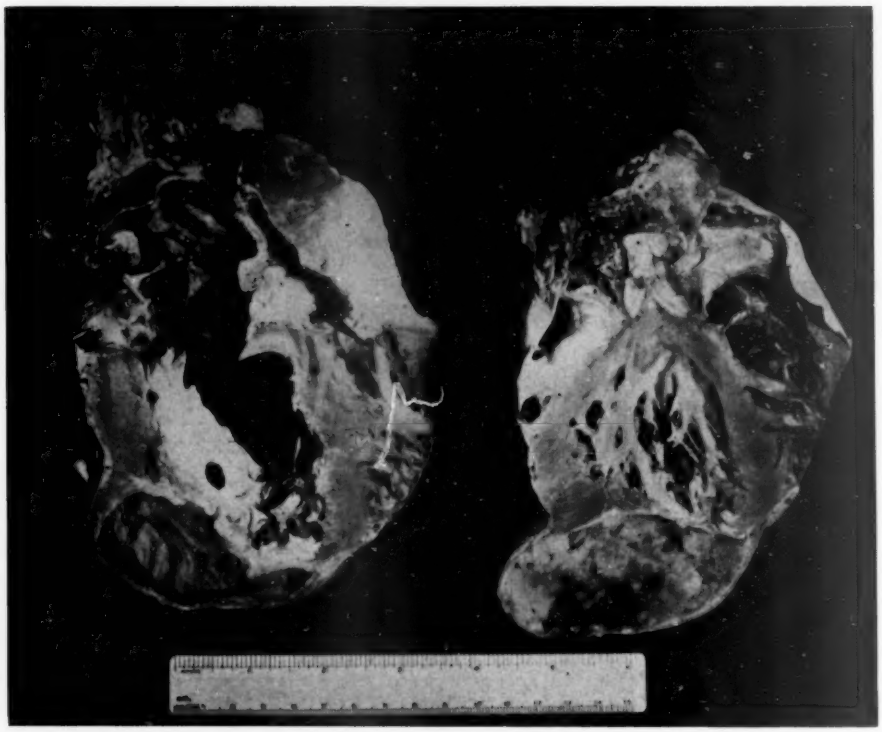

FIG. 1. Section through the ventricle showing the thickened endocardium with the small annular opening communicating with the aneurysmal sac below. Note the dense laminated clot in the sac on the left. The clot has been removed on the right. The characteristic incisura is seen on the right. Figures 5 and 6 are roentgenograms of this case.

within the sac and tend to prevent rupture. The sac usually consists of the endocardium, the damaged myocardium and both layers of the pericardium.

In one of the cases, the endocardium was thickened and communicated with the aneurysmal sac through an opening 8 mm. in diameter (Fig. 1). The sac measured 8.5×4 cm. and was filled with a well organized, laminated clot.

In the other (Fig. 2), a thickened ridge of endocardium surrounded the ventricular cavity at the junction of the lower and middle thirds of the left ventricle with an expanded tip measuring 7×3.5 cm. occupied by a degenerating, well organized clot. The wall of the sac was composed of endocardium, both pericardial layers and the parietal pleura. The myocardium was replaced by fibrous tissue in both cases.

Only Schwedel and Gross,[12] in the literature reviewed, emphasize the frequency and importance of associated pleuropericardial adhesions as of diagnostic significance. The location and extent of the initial anemic infarct are the important factors in the formation of adhesions. Large infarcts may involve the cardiac myocardium to a considerable degree without bulging or a tendency toward the formation of an aneurysm (Figs. 3 and 4).

ROENTGEN FINDINGS

The roentgenological findings in ventricular aneurysms with bulging are quite characteristic. There is a definite bulging deformity of the cardiac outline that is always a part of the cardiac shadow appreciable in various positions (Figs. 5 and 6). An incisura may or may not be seen separating the bulge from the remainder of the shadow. If the orifice into the sac is adequate and the clot is not too dense, roentgenoscopic examination will disclose a paradoxical pulsation within the sac that causes it to expand during systole and decrease in size

during diastole. This sign is pathognomonic of ventricular aneurysm but is not always seen. The contrapulsile phenomenon must be definitely expansile in character and not confused with the tilting distortions due to the pericardial adhesions. One of our cases (Fig. 7) when first observed showed abnormal pulsations of this type that gradually disappeared during the course of the disease most probably due to an increase in the density of the thrombus and the fibrosis of the aneurysmal wall.

Aneurysms at or near the apex are readily detected both on the anterior and posterior walls. There may be a bulge of considerable size near the auriculoventricular junction that may not be differentiated from the dilated cardiac contours (Fig. 8).

It has been pointed out by others[12] that myocardial infarction that has undergone contraction may make the normal cardiac musculature appear to bulge, simulating ventricular aneurysms. Pericardial adhesions are seen in both conditions. It has been noted that calcium is frequently deposited in the pericardiopleural adhesions. Deposits in chronic infarction (Fig. 4) lie deeper within the cardiac border than those in aneurysm (Fig. 5). This, together with the associated bulge in the cardiac outline, will differentiate these conditions as well as calcified pericardium.

Bulges of the cardiac shadow near the base are generally due to dilatation of the pulmonary conus, Ayerza's disease, dilatation of the sinus of Valsalva or rarely coronary aneurysm (Figs. 9 and 10).

The strength of the scar tissue, character, age and location of the lesion are factors in determining the extent of the bulge. Aneurysms at or near the apex are possibly subjected to greater intraventricular pres-

Fig. 6. The aneurysmal sac is the expanded tip of the left ventricle. Note the thickness of the sac and the thickened endocardium on the left. A degenerating blood clot is seen in the sac on the right. The incisura is not well defined. Figures 7 and 11 are roentgenograms of this case.

Fig. 3. Section of the left ventricle showing extensive cardiac infarction due to coronary thrombosis without a tendency toward bulging or the formamation of an aneurysm. Calcific deposits lie deep within the infarcted area. Figure 4 is the roentgenogram of this case.

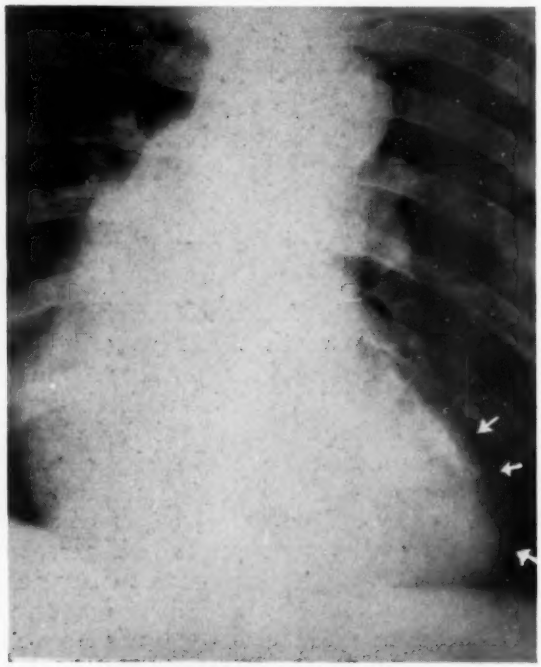

Fig. 4. Same case as Figure 3. Note the depth of the calcific deposits within the cardiac borders and the absence of bulging.

Fig. 5. Same case as Figure 1. The cardiac deformity is characteristic. A thin line of calcium deposited in the wall of the sac (black arrows).

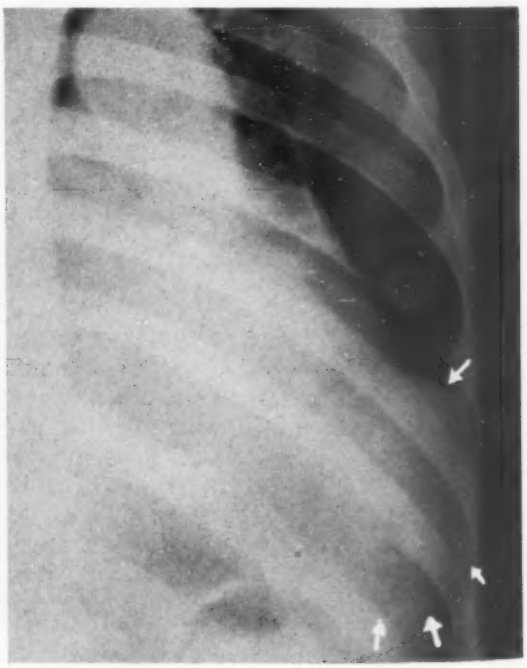

Fig. 6. Same case as Figures 1 and 5 in oblique view disclosing constant deformity, pleuropericardial adhesions and calcium deposits in the aneurysmal sac.

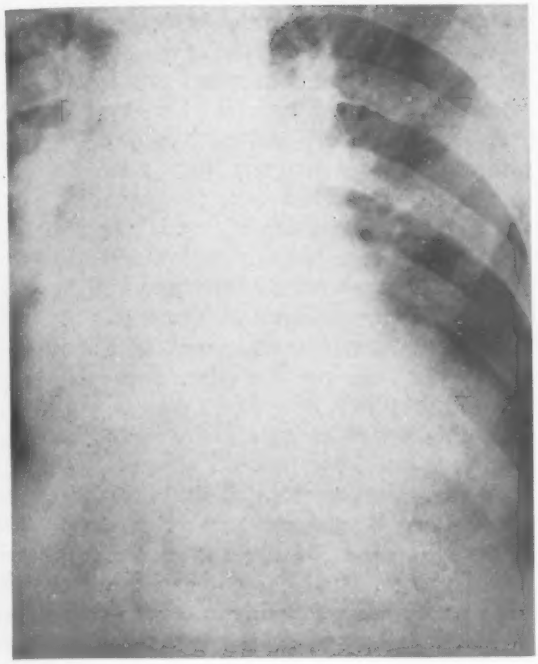

Fig. 7. Same case as Figure 2. The incisura in the left cardiac border was well defined in vivo.

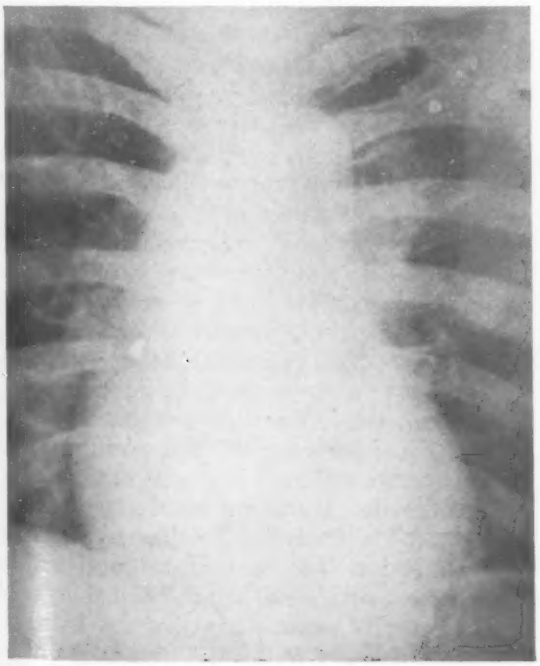

Fig. 8. Roentgenogram of a case of coronary disease with a marked thinning of the left ventricle and considerable bulging near the auriculoventricular junction that cannot be distinguished from the normal cardiac contour.

Fig. 9. Roentgenogram of a case with aneurysmal dilatation of the right coronary artery disclosing a deformity in the region of the conus.

Fig. 10. Sectioned heart in Figure 9 showing the enormous expansion of the ostium of the right coronary artery and the aneurysmal dilatation.

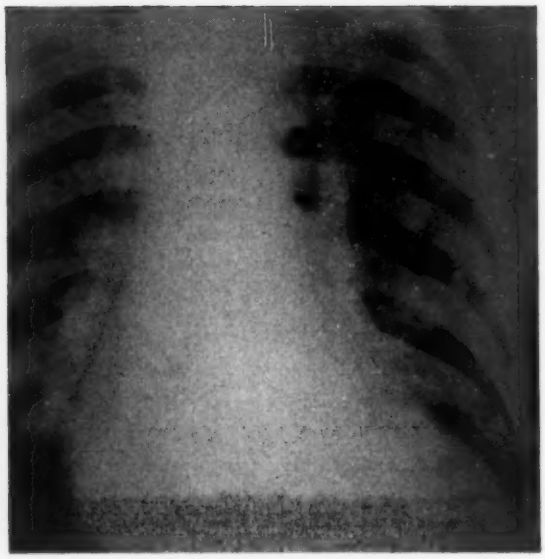

FIG. 11. Same case as Figure 7 two years later showing no apparent change in the size of the aneurysmal bulge despite a definite increase in the size of the cardiac shadow subsequent to progressive heart failure.

sure during systole than those near the base. Small aneurysms within the myocardium are not demonstrable roentgenologically. In our cases there was practically no change in the size and contour of the sacs over periods of three and four years despite the increase in the size of the heart subsequent to progressive cardiac failure (Fig. 11). There was seen, however, an increase in the extent and density of the calcium deposits in the pericardiopleural adhesions.

CASE REPORTS

CASE 1. H. Y. (No. 15662), admitted on January 5, 1933, aged thirty-eight, complaining of pain in the region of the heart, dyspnea and a "dead feeling in the right arm." Fifteen months prior to admission he had experienced severe pain in the region of the heart and marked prostration. He also had pain in the right arm. Syphilis was contracted in 1919. The amount and character of the treatment were unascertainable.

The patient was weak and dyspneic but not edematous on admission. Heart was enlarged with a blowing systolic murmur at the apex. Wassermann 25 per cent; Kahn 4 plus. Blood picture was not remarkable. Electrocardiogram: Lead I, QRS upright, P upright, P-R interval .18 sec.; Lead II, QRS upright, "R" notched, T inverted; Lead III, QRS upright, P-R interval .20 sec.; "S" notched and T inverted. Roentgenogram disclosed the peculiar conformation of the cardiac shadow. The patient complained frequently of gastric distress and had several asthmatic attacks described as typical. Improved under bed rest and medication. Discharged on February 23, 1933.

There were readmissions on October 5, 1934, August 18, 1935, March 5 and July 21, 1936, with an average hospitalization period of two months. On each return there was a slight exaggeration of the symptoms. There was evidence of marked decompensation with occasional syncopic attacks on the last admission. He died on July 24, 1936.

Postmortem Findings. There is an enormous enlargement of the heart. The thoracic viscera maintain a normal relationship otherwise. The prepericardial tissues are edematous. The pericardium is thin. The sac contains approximately 50 cc. of a clear amber fluid. The walls are smooth and glistening except over the apex where firm, fibrous adhesions attach both pericardial layers and the pleura to the anterior chest wall. The heart measures 21 cm. in situ (oblique diameter) and weighs 950 gm. There is a bulbous enlargement of the apex that is adherent to the anterior chest wall and reduces a small portion of the left lower lobe to a thin atelectatic band. The right side of the heart is dilated. There is an increase in the size of the pulmonary conus and artery.

The aorta is broadened throughout the ascending and transverse portions of the arch. The epicardium shows patches of thickening. The coronary arteries are markedly sclerotic. The apex is thin and fluctuant with calcified deposits within the walls of the sac. Proximal to the bulbous portion, the wall of the left ventricle has a zone of constriction that extends to the septum but does not involve the right ventricle. On section, the left ventricle has a thickened endocardial floor containing a circumscribed annular opening 8 mm. in diameter that communicates with the aneurysmal sac which is 8.5×4 cm. The sac is filled with a degenerating laminated clot. The ventricular wall proper measures 1.5 cm. in thickness. The aneurysmal sac is less than 1 mm. thick. All of the chambers contain slow-forming clots. The aortic valves are thickened and sclerotic. There are no vegetative lesions. There is a narrowing of the coronary ostia. Extensive scars, ulcerations and striations are seen in the aorta, mostly in the area of the fusiform enlargement involving the first part of the arch. Extensive calcific deposits are seen throughout.

Both lungs show considerable congestion with beginning hypostatic pneumonia in the right lower lobe. The abdominal cavity contains approximately 1 liter of a deep amber clear fluid. There is no intrinsic pathology in the gastrointestinal tract. The liver is moderately cirrhotic. The kidneys show a moderately severe arteriosclerotic nephritis. No other gross pathology noted.

The cause of death may be ascribed to congestive heart failure with aneurysms of the left ventricle and aorta.

Microscopic Findings. Sections of the heart show an obliterating endarteritis involving the arteries. Many of the arterioles are occluded by organized thrombi. There is a marked increase in the interstitial fibrosis. The muscle fibers are fragmented with faintly staining nuclei. A moderate round cell infiltration is seen about the vessels.

The sac is composed of dense fibrous tissue. A few fragments of degenerated muscle fibers are seen near the periphery. Spirochetes are not demonstrable by the Sperry-Warthin method of staining.

Case II. J. C. S. (No. 9494), aged forty-one when admitted on September 2, 1932, complained of shortness of breath, pain in left chest and shoulder. Had gastric distress with occasional vomiting. Present illness began early in 1932 with marked general weakness, shortness of breath and pain in both shoulders and back. Feet were swollen in 1931. Had occasional "heart flutter."

Penile sore in 1916. Received indeterminate amount of treatment. Physical examination: Patient apparently weak and ill, is fairly well nourished with a slight infraorbital edema. Point of maximum intensity of the cardiac pulsation displaced downward and out in the sixth intercostal space 3 cm. outside the mid-clavicular line. First sound is displaced by a distinct blowing murmur followed by a less pronounced diastolic murmur. All sounds are weakened but more distinct at the base. A-2 is accentuated. Pulse is small and of poor volume. Blood pressure 118/80. No other significant pathological findings are noted.

Wassermann 75 per cent fixation, Kahn 4 plus. Renal function showed a total of 86 per cent in two hours. Roentgen examination disclosed the peculiar conformation of the cardiac shadow. Under bed rest, digitalis and specific medication, the condition improved. The patient was discharged on December 8, 1932.

He was readmitted on September 21, 1934, with an exaggeration of the old symptoms. During roentgenoscopic examination, the paradoxical character of the pulsations of the cardiac apex was noted. After prolonged hospitalization, the condition gradually grew worse. Electrocardiogram, February 26, 1936: T-I, inverted, T-II and T-III upright, QRS upright .06 sec., very low voltage, frequent extrasystole; QRS-II inverted, QRS-III upright, notched and extrasystoles. P-R interval .2 sec., P upright in all leads.

The general course was downward with increasing pain in the region of the heart, gastric distress and pain in the lumbar region. Semicomatose on June 16, 1936. Died June 20, 1936.

Postmortem Findings. The pericardium is thickened. The walls of the sac are smooth except for an area 1 cm. in diameter in which the pericardium is adherent to the left ventricle by fibrous bands. Similar adhesions fix the pleural surface superjacent to this point. The sac contains 20 cc. of a clear amber fluid. The pleural surface shows injection of the superficial vessels.

The heart measures 16 cm. in situ (oblique diameter). There is a bulbous deformity at the apex of the left ventricle with a deep indentation stopping apparently at the interventricular septum. There is a narrow groove separating the bulbous apex from the remainder of the left ventricle. The apex is ischemic and soft. The right ventricle is small but the walls are hypertrophied. On section, the apex is occupied by a laminated pale clot, the center of which is soft and of a dark red color. Contiguous with the fibrous tissue that marks the upper limits of the apical dilatation externally is seen a dense fibrous ring in the intima 2 cm. in diameter that represents the orifice of the aneurysmal sac. The musculature of the left ventricle measures 1.5 cm. in thickness. It is pale and contains small grayish streaks. White patches are seen in the pectineal muscles. The aneurysmal sac is thinned to 1.5 mm.

The aortic leaflets are thickened but remain competent to the water test. There are no vegetative valvular lesions. The aorta shows a few yellow atheromata but no scars or striations. The coronary arteries are small and markedly sclerotic.

Both kidneys show extensive damage consequent to a severe arteriosclerotic nephritis. The remaining organs disclose no significant pathological changes.

The cause of death was ascribed to coronary thrombosis, a severe arteriosclerotic nephritis,

and aneurysm of the left ventricle.

Microscopic Findings. A section of the heart muscle shows a thickening of the epicardium. The fibers are less densely stained over large areas. There is an interstitial fibrosis. The larger vessels show obliterative endarteritis and some are thrombosed. Under high magnification there is considerable fragmentation of the muscle fibers. Occasional nuclei are deeply stained. Some of the cells show brown atrophy. Many of the small capillaries are obliterated and some are reduced to fibrous bands. Slight lymphocytic infiltrations are seen but are not confined to the perivascular structures.

SUMMARY

1. Ventricular aneurysms subsequent to coronary disease and thrombosis are rarely diagnosed in vivo because the diagnostic criteria are insufficiently specific.

2. The severity of the symptoms in the acute form precludes the manipulations necessary for adequate roentgenological studies.

3. In the chronic form, the onset gives rise to acute symptoms which are later overshadowed by the signs and symptoms of cardiac failure.

4. A definite persistent bulging of the cardiac contours must be favorably situated for observation.

5. A history of an early, sudden, precordial pain radiating to the shoulder with marked prostration showing a gradual recovery from the acute symptoms followed by indications of a damaged myocardium should lead to a careful roentgenoscopic examination to detect any abnormalities in the cardiac contour.

6. The early presence of pleuropericardial adhesions in the absence of a bulge most probably indicates an infarct rather than aneurysm.

7. The pathognomonic contrapulsile phenomenon can be demonstrated only when the aneurysmal sac is incompletely filled by the clot.

8. Chronic aneurysm, once developed, shows little change in size or shape despite the gradual enlargement of the heart as the result of a progressive cardiac failure.

9. It would appear from the cases here presented that syphilis plays no part in the formation of chronic ventricular aneurysms.

10. There are reported here two cases of aneurysm of the left cardiac ventricle in syphilitic individuals which were diagnosed in vivo and confirmed at necropsy.

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PERICAPSULAR OSSIFICATION OF SHOULDER

REPORT OF CASE

By HOMER W. GRIMM, B.Sc., M.D.
PITTSBURGH, PENNSYLVANIA

THE patient, Z.I., female, aged twenty-eight, was in an automobile accident July 27, 1936, in which she was thrown a distance of approximately 50 feet. She was discharged after being in a hospital eight days. The shoulder was roentgenographed at the time of discharge and she was notified later that she had a subglenoid dislocation of the left shoulder. The patient entered a second hospital where roentgenograms were made of the left shoulder, revealing a subcoracoid dislocation which had occurred two weeks previously. There was also a fracture of the greater tuberosity of the left humerus.

FIG. 1. August 8, 1936, before reduction.

On August 12, 1936, following two unsuccessful attempts at closed reduction, open reduction was done, capsulorrhaphy.

Gross Pathology. The head of the humerus is in a subcoracoid position and the greater tuberosity has been fractured, and lies about 1 inch posterior to the humerus.

The patient was discharged on August 18, 1936. She still complains of pain in the wound. Subsequent films show pericapsular ossification and bony ankylosis of the parts. The cause of the condition is apparently trauma with pericapsular hemorrhage which became ossified.

I have been unable to find a description of this condition in the literature.

FIG. 2. September 19, 1936. after reduction showing beginning pericapsular ossification.

FIG. 3. May 21, 1937, showing late pericapsular ossification.

CARCINOMA OF THE HEAD OF THE PANCREAS

REPORT OF A CASE

By JAMES M. FLYNN, M.D.
ROCHESTER, NEW YORK

MRS. E. C., referred by Dr. L. for roentgen examination of the gastrointestinal tract, May 29, 1936.

White female, aged forty-two, well developed. Complained of nausea and vomiting and abdominal cramps with loss of weight. Onset in March, 1936; prior to that time, patient was in good health. In March, 1936, she noticed that she felt nauseated and that everything she ate seemed to regurgitate. She claimed that she vomited more than she ate. Even the sight of food caused her to become ill. Cramps seemed

FIG. 1

at first to be localized in the upper gastric region, later became generalized and persisted until two weeks before patient was referred. Examination showed the following:

Past history was negative and irrelevant.

Head: Eyes, ears, nose, mouth and neck, negative.

Chest: Lungs, clear and resonant; no râles heard. Heart, rate, rhythm and tone good; no murmurs.

Lymph nodes: None palpable.

Extremities: No edema; no clubbing. Reflexes normal.

Roentgenoscopic and roentgenographic examination of the gastrointestinal tract revealed an obstruction in the second portion of the duodenum, with considerable gastric retention. A tentative diagnosis of cancer of the head of the pancreas was made at this time.

The patient was referred to a surgeon, Dr. S., who performed a laparotomy on June 4, 1936. The report on the chart is as follows:

Stomach dilated and obstructed by a round, hard mass in the duodenum which feels like a stone. Did not disturb questionable stone. No enlarged glands in the region. Gallbladder inflamed and contains large stones. No other pathological condition. Posterior gastroenterostomy and cholecystectomy performed. Patient remained in the hospital for seventeen days and was discharged after an uneventful recovery.

Patient began to have attacks of pain in the abdomen in February, 1937, with noted change in her color, a jaundiced condition being observed later. There was also an itching of the skin and continued loss of weight. She returned to the hospital on April 18, 1937. A second laparotomy was performed on April 19, 1937, by the surgeon who had performed the previous operation. The report on examination follows:

Large mass in the head of the pancreas with a thickening throughout the pancreas. Common duct greatly dilated. Unable to pass probe into duodenum. No stone palpated after a serious effort to do so. Specimen removed for biopsy. Drainage into common duct with a T-tube, cig-

FIG. 2

arette drains brought out through stab wound.

Pathological report of biopsy reads as follows: Bit of pancreas, roughly 1×1×1 cm., bits of skin 0.6×7 cm., 0.8×4 cm., scar tissue with fat attached. Diagnosis: Adenocarcinoma.

The patient died on April 27, 1937. Cause of death was given as carcinoma of the pancreas.

The reason for presenting this interesting case is that, irrespective of the diagnosis and conclusions rendered by the roentgenologist, the surgeon disregarded the idea of cancer at the time of the first operation, assuming that the obstruction was caused by an impacted gallstone and not by a then localized new-growth in the head of the pancreas.

RADIATION THERAPY IN CANCER OF THE SKIN*

By BERNARD PIERRE WIDMANN, M.D.
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A PROCEDURE for treating cancer of the skin with low voltage (75–135 kv.) roentgen rays or radium is described herein. A specific dosage formula admits of a simple, effective and universal method according to the thickness or approximate bulk of the lesion, regardless of the size of the surface area, the size being estimated as shallow or large if it is less or greater than 0.5 cm. elevation above surrounding normal skin surface. The skin erythema dose (S.E.D.) is considered as representing 500 r and this arbitrary factor is used to denote a skin unit value, so that the total intensity of roentgens will indicate so many multiples of a skin erythema dose for relative and comparative estimations.

The technique is an evolution and summation of ten years' experience at the Philadelphia General Hospital, and it is an outgrowth of attempts to formulate doses to effect palliative regressions of advanced, fungated, inoperable superficial cancers, particularly of the breast. The results were correlated according to tissue repair with varying intensities and rates of distribution. There were sufficient data and clinical experiences to formulate opinions and conclusions regarding the probable maximum normal tissue and tumor tolerance within the limits of the technique prescribed.

Cancer of the skin has been controlled successfully by surgery, electrodesiccation, roentgen rays, and radium. Irradiation is frequently used in combination with electrosurgical measures. There is now a strong tendency to confine the treatment entirely to irradiation and especially to low voltage or soft or long wave length radiations (factors according to Table 1).

There is a manifold variety of techniques of massive and fractional doses of low voltage (60–135 kv.) roentgen rays (soft or long wave length radiations 0.3 to 0.55 Å), which show consistently good results in experienced hands. None of these procedures are new. And practically every radiologist has a favorite technique or formula for treating cancer of the skin, which he has mastered and which is effective and enables him to duplicate good results.

Unfortunately, many clinics operate on empirical procedures. Such a program of attempted individualization or of meeting in a particular way the problems of a particular case have given rise to trying situations in our own clinic. The associates and students were constantly harassed by the apparent tremendous uncertainties and indecisions. The many methods accomplishing equally good results created an atmosphere of perplexity. The wide latitude of doses and the good results were accepted in amazement and seemed to indicate the use of an acquired art and experience which the student must strive to achieve in the years to come.

There is, obviously, great need for a simplified accurate conservative technique that will eliminate hair-splitting differences and possible errors, due to the element of personal equation, in measuring or estimating the size of a lesion. An attempt has therefore been made to establish an understandable uniform working basis of a technique of radiation treatment of cancer of the skin. The procedure described is simple, speedy, effective, and economical. Adjustments must be made in some cases and further experience may evolve additional advantages in change of rate, distribution and intensity.

Experiences in treating superficial cancers of wide and deep involvement with low voltage (approximately 125 kv.) roentgen rays were reported by me[20,21] in 1932 and

* From the Radiological Department of the Philadelphia General Hospital, Philadelphia, Pennsylvania. Read at the Fortieth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 19–22, 1939.

1934. Much of the material concerned extensive fungating and inoperable growths. Some were 10 to 15 cm. in diameter. Every conceivable combination of rate of distribution and intensity was employed. Total doses of 2,500 to 10,000 r were given within periods of one to four weeks.

There are voluminous reports in the literature showing good results with doses ranging from 1,500 to 10,000 r. The rate varies from massive treatment given at one time to divided daily doses of 200 to 500 r or 500 to 1,500 r or similar doses two or three times a week.

MacComb[10] reported uniform control of lesions 1.5 cm. in diameter with a single dose of 6,500 r, and gave as much as 10,000 r to lesions 1 cm. in diameter without deleterious skin effects.

Harvey, Dresser and Warren[7] demonstrated similar effects of radiation produced at 50, 90, 200, and 1,000 kv. It required approximately 6,000 r to obtain a complete lethal effect upon the Brown-Pearce rabbit epithelioma, which they observed to be a tumor consistently resistant to roentgen irradiation during more than three years' work in their laboratory.

Lawrence, Horn and Strong[9] irradiated a theelin induced mouse mammary adenocarcinoma with various doses of filtered 200 kv. roentgen rays and determined the lethal dose to be approximately 4,500 r.

Sugiura,[18] using roentgen rays generated at 200 kv., found the lethal dosage for mouse sarcoma 180 to be 2,800 r.

Packard[13] irradiated mouse sarcoma 180 with both high and low voltage roentgen rays and concluded that the lethal dose was about 2,700 r. He also concludes that both high and low voltage roentgen radiation are equally effective.

Paterson[14] feels that the lethal dose for a true squamous cell epithelioma will ultimately be proved to be, for any one fixed over-all time, a remarkably constant figure, regardless of where the tumor is situated, and that it probably ranges from 5,000 r in a week to 6,000 or 7,000 r in one or two months.

Bromley[2] reports experience with a Chaoul tube. Doses of 400 r were given daily for a total of 6,000 r. Occasionally 2,000 r in one treatment controlled a basal cell carcinoma (60 kv., 0.2 mm. Ni or Cu, half-value layer 0.1 mm. Cu, 0.3 Å, portal 5 cm. in diameter, distance 5 cm., 4 ma., rate intensity 80 r per min.).

Bromley[1] also observed that even when for various reasons the Chaoul beam has been found to cause necrosis of tissue, the effect is very strictly localized and the recuperative powers of the immediately adjacent tissues are unaffected.

Den Hoed,[8] using a Metalix contact therapy tube, gave doses varying from 1,700 to 7,000 r, depending upon the estimated thickness of the tumors. The average lesions required 3,000 r. All histologic types responded equally well. Treatments were routinely given at one sitting.

Van der Plaats[19] attempted to estimate the depth of a lesion and give 3,000 r at 1, 2, 3 or 4 cm. depth. This would necessitate a cross-fire direction of the beam so that a lesion 1 cm. in diameter would require a surface dose of 15,400 r to deliver 3,000 r at 1 cm. depth; a lesion 2 cm. in diameter would require 47,000 r on the surface to obtain 3,000 r at 2 cm. depth; and a lesion 3 cm. in diameter would require that 120,000 r be directed through multiple fields in order to obtain an intensity of 3,000 r at 3 cm. depth. He has chosen to call this technique the "x-ray caustic method." (Factors: 50 kv., 2 ma., half-value layer 0.3 mm. Al, 2 cm. focal skin distance. The dosage rate is 8,000 r per min. The cone diameter is 10 mm.) This technique is carried out in one application.

Carty and Ray[3] studied the effects of low voltage (60 to 80 kv., 0.5 mm. Al filter equivalent in oil) roentgen rays on the brains of dogs. While 6,000 to 12,000 r at the rate of 2,000 r per treatment showed microscopic changes in the brains at autopsy, it required 12,000 r before clinical effects of lethargy, anorexia and vomiting occurred. The microscopic changes in degenerated cells at two weeks were progres-

sively marked for 6,000, 12,000 and 18,000 r, the last dose producing extensive edema, hemorrhage and cell degeneration extending to the opposite hemisphere of the brain.

Driver and Cole[6] reported good results of low voltage radiation (133 kv.) in epitheliomas of the eyelid, with divided doses of 800 to 1,000 r every second day for total doses of 3,200 to 6,000 r, part of the treatment given with no filter and part with 1 or 2 mm. Al filter.

Cutler[5] obtained regressions with 1,000 to 3,000 r (measured on the skin) in one to two treatments. This dose caused an intense inflammatory reaction of the irradiated area, at times followed by superficial necrosis during the second or third week after treatment. After four to five weeks cicatrization was usually complete.

These great differences undoubtedly have significant clinical importance. They are not readily adjustable to the clinical results. It is therefore expedient to establish a predetermined dose that will allow for differences of sensitivity or resistance, the conditions of resistance to be met by additional treatment. This eliminates the hazards of bad results due to excessive treatment.

If the radiation treatment of cancer of the skin were to be confined to lesions 0.5, 1.0 and 1.5 cm. in diameter, then doses of 6,000 r could be given, provided there was considerable thickness of exuberant as well as subcutaneous involvement and the field of irradiation sharply localized to the lesion. The inclusion of a sufficiently wide margin of skin will insure a more certain control and show a good cosmetic effect with half this intensity, according to the experiences and technique described later. For the very fungating lesions with an obvious elevation of tumor tissue of 1 cm. or more above the surrounding skin margin, at least 6,000 r and frequently as much as 10,000 r may be necessary (Fig. 1).

FIG. 1. The depth of the tumor is generally commensurate with the progressive increase in the surface area and this precludes any attempt at a mathematical estimation of the degree of marginal or depth permeation or infiltration.

DOSAGE CONSIDERATIONS

The dose value must always be expressed in roentgens as well as the factors of voltage, distance, filter, size of irradiated field, half-value layer, and effective wave length, as well as the rate of distribution and intensity; and type of rectification and designation as to an open or an oil-immersed tube are likewise important.

Ionization measurements or the half-value layer determinations must be made regularly, because fluctuating currents, faulty meters, and variable glass wall thickness of the tubes, as well as the extent of metallic coating on the walls from pitting of targets due to hard and prolonged use, are matters that seriously alter the output of radiation.

Chart 1 illustrates the absorption curves for low voltage (60 to 125 kv.) roentgen rays with no filter and with 1 mm. Al filter, as compared to the Chaoul tube and radium bomb (5 cm. distance). About 46 per cent of the surface intensity of low voltage roentgen rays will reach a depth of 3 cm. with no filtration, as compared to 62 per cent with 1 mm. Al filtration. Approximately one-half of the unfiltered radiation is absorbed in the first 2.5 cm. of tissue, whereas approximately 4 cm. of tissue is necessary to absorb one-half of the radiation with 1 mm. Al filtration.

The physical characteristics for different voltages and filtrations (according to Weatherwax) are shown in Table 1.

Table II (by Weatherwax) shows the depth dose variations for target-skin distances of 20, 30 and 40 cm. The differences are slight and for clinical purposes and in

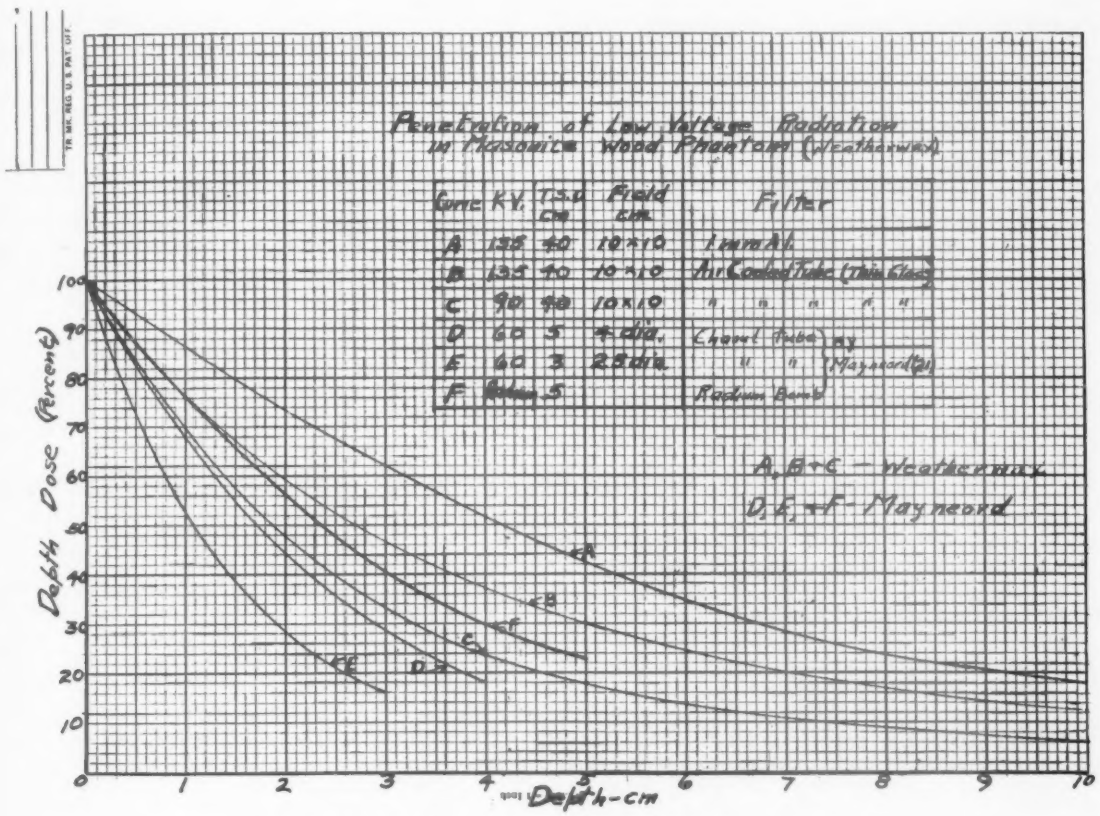
Penetration of Low Voltage Radiation
in Parallel Wood Phantom (Weatherwax)
Depth Dose (Percent)
Depth-cm
A, B + C — Weatherwax
D, E + F — Mayneord

CHART 1. Absorptive curves for low voltage roentgen rays.

the magnitude of doses generally used are probably not significant. The values change appreciably with 1 mm. Al filtration. The dose at 3 cm. depth increases about 10 per cent at 30 cm. distance with 1 mm. Al filtration.

There is comparatively a slight difference in penetration for different sizes of fields ranging from 4×5 cm. to 6×8 cm. and 10×10 cm. for the depth doses ordinarily necessary for practical use in treating superficial lesions.

Surface applications of radium and the Chaoul tube therapy give very similar absorption curves (Chart 1), but the penetration is markedly less as compared with low voltage (90–135 kv.) roentgen rays. For superficial lesions the clinical results are comparable. For the large fungating inoperable lesions, for which irradiation is nearly

TABLE I

Kilovolts	Filter	Half-Value Layer	Effective Wave length
135	None	1.0 mm. Al	0.55 Å*
135	1 mm. Al	2.3 mm. Al	0.41 Å
135	2 mm. Al	3.9 mm. Al	0.32 Å
100	None	7–8 mm. Al	
90	None	0.67 mm. Al	0.60 Å
90	1 mm. Al	1.8 mm. Al	0.44 Å
90	2 mm. Al	2.4 mm. Al	0.38 Å

(All measurements in air. Air-cooled universal tube.) (Rate intensity 210 r per min., with 125 kv., 30 cm. distance, 10×10 cm. field.)
*Ångström = 000.000.01 cm. or 10^{-8} cm.

Table II

10×10 cm. field, 130 kv.

Masonite Wood Phantom Depth in cm.	Unfiltered Radiation			Radiation Filtered by 1 mm. Al		
	Target-skin Distance 40 cm.	Target-skin Distance 30 cm.	Target-skin Distance 20 cm.	Target-skin Distance 40 cm.	Target-skin Distance 30 cm.	Target-skin Distance 20 cm.
Half-submerged	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
1 cm.	76.0	74.0	72.5	86.0	84.5	82.0
2 cm.	59.0	57.0	53.7	74.0	71.5	67.3
3 cm.	46.0	44.0	40.0	62.0	63.5	55.0
4 cm.	37.0	31.0	31.0	52.0	49.0	43.7

always of only palliative benefit, low voltage roentgen rays are of undoubted superior value.

The factors used in the Chaoul therapy[4] are: 60 kv., 0.2 mm. Ni or 0.2 mm. Cu filtration, effective wave length 0.3 Å, half-value layer 0.1 mm. Cu or 3.3 mm. Al, 4 ma., and 3 to 5 cm. target-skin distance. For contact applications the dosage rate is approximately 800 r per minute; for a target-skin distance of 3 cm. approximately 88 r per minute, and at 5 cm. distance approximately 36 r per minute. The effective wave length approximates the values obtained with 135 kv. and 2 mm. Al filtration. The penetration with 100 to 135 kv. is considerably greater because of the greater target-skin distances commonly used with the air-cooled and also the more recently developed oil-cooled shockproof tubes.

Van der Plaats[19] gives factors equivalent to 0.2 mm. Al filtration, half-value layer 3 mm. Al, 2 ma., intensity at 2 cm. distance from focal spot 8,000 r per minute. The depth dose at 1 cm. is approximately 20 per cent and at 2 cm. about 7 per cent, with little difference for areas 1 and 2.5 cm. in diameter.

Den Hoed[8] reports similar experiences with the Metalix tube and finds little difference in the absorption curves compared with radium applicators 3×4 cm. directly on the surface, and slight but no practical increase of radium-ray penetration at 1 cm. distance. His measurements show a depth dose of 33 per cent of the surface intensity at 1 cm. depth and 13 per cent at 2 cm.

Skin Erythema Dose

The ultimate value of a dose of roentgen rays must be indicated in terms of roentgens. The demonstrable biological effect is a skin reaction. A slight reaction of the skin that will appear in 80 per cent of the cases, in ten to fourteen days, has been defined by Quimby[15] as a threshold erythema dose (T.E.D.)

MacComb[10] describes a threshold erythema as that quantity of radiation which produces in 80 per cent of all patients treated a visible pigmentation within one month and in others no visible reaction. He determines 350 r as the threshold erythema dose value for areas of 0.5 to 2 cm. in diameter and 280 r for areas 3 to 5 cm. in diameter. With these factors no satisfactory regression occurred with less than 12.5 T.E.D.

Reisner[17] considers 450 r as the skin erythema dose for 75 kv. (half-value layer, 0.4 mm. Al) for a 2×2 cm. field.

MacKee and Cipollaro[11] interpret a threshold erythema as 212 r, which appears in seven to ten days and persists about two weeks by thermionic rectification, and identical effects from 266 r by mechanical rectification. (Areas 2.5 cm. sq., unfiltered radiation, 80 to 100 kv., measured in air.)

There is a great difference of opinion as to the degree of skin reaction from 200 to 800 r indicated in a voluminous report of experiences in the literature, but frequently data are lacking about the region, size of area, quality of radiation, voltage, etc.

The fact that there is no agreement on the intensity and duration of the skin reactions of redness and pigmentation shows that the effect is not fundamentally important from the standpoint of end-results, provided the requirements of a standardization are fulfilled and the designation of dosage in terms of roentgens is maintained.

The purposes of teaching are more readily attained by associating the dose in roentgens with the biologic skin reaction of erythema. Like the grains, ounces, etc., of a pharmaceutical formula based upon physiologic effects and tolerance, the unit of skin erythema dose not only indicates a basis of biologic standardization but also implies a reliable method of comparison, so that the total roentgens will be considered as consisting of so many multiples or units of a biologic skin reaction or skin erythema dose.

For simplicity and uniformity the skin unit was arbitrarily selected as represented by 500 r (1 S.E.D.). One might just as properly prefer 200, 300 or 400 r. The practical difference for computation is of no importance because the skin effect of 500 r (1 S.E.D.) is identical with the skin effect of 500 r (2 S.E.D.)—fields 0.5 to 1 cm. If the terminology is adhered to in each department it will serve the purpose of indicating the proportion of doses in so many multiples of skin units.

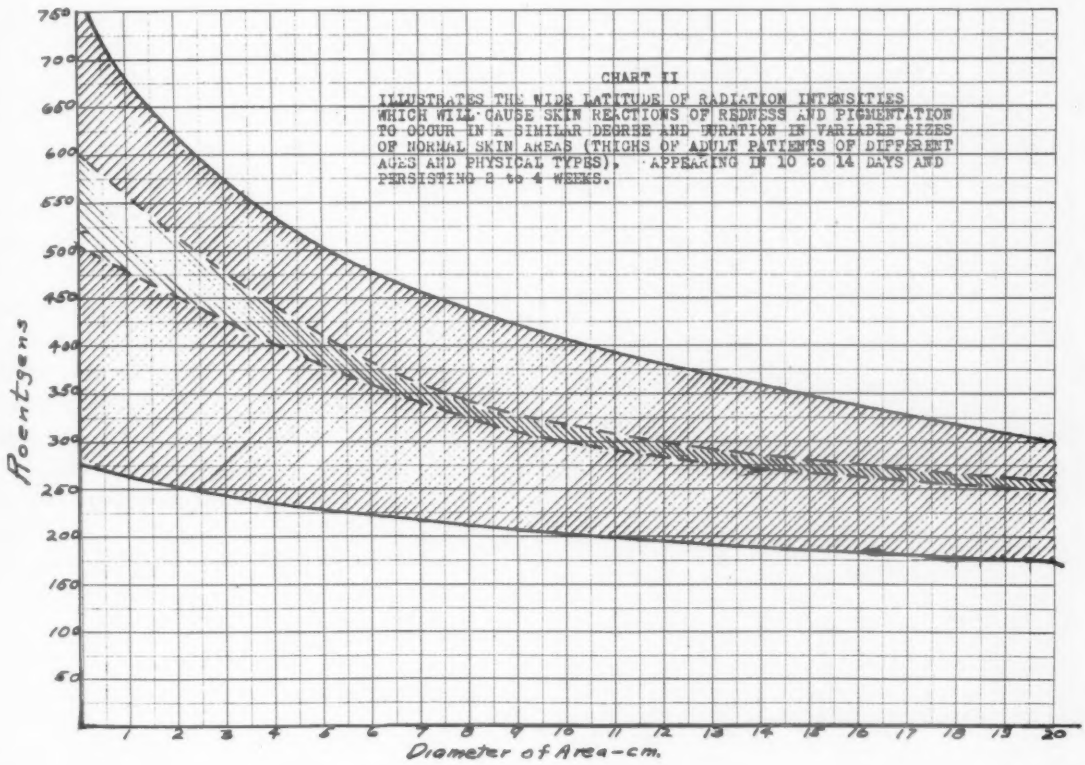
CHART II
ILLUSTRATES THE WIDE LATITUDE OF RADIATION INTENSITIES WHICH WILL CAUSE SKIN REACTIONS OF REDNESS AND PIGMENTATION TO OCCUR IN A SIMILAR DEGREE AND DURATION IN VARIABLE SIZES OF NORMAL SKIN AREAS (THIGHS OF ADULT PATIENTS OF DIFFERENT AGES AND PHYSICAL TYPES), APPEARING IN 10 to 14 DAYS AND PERSISTING 2 to 4 WEEKS.
Roentgens
Diameter of Area-cm.

CHART II. Illustrates the wide latitude of radiation intensities which will cause skin reactions of redness and pigmentations to occur in a similar degree and duration in variable sizes of normal areas (thighs of adult patients of different ages and physical types), appearing in ten to fourteen days and persisting two to four weeks.

Chart II illustrates the wide latitude of equal skin effects that are obtained with different sizes of irradiated areas and varying intensities. The curve representing the wide zone of pigmentation of the skin has been estimated on the basis of skin tests made almost yearly for the past ten years with different technical factors of long wave length radiations as indicated in Table 1.

It was exceedingly difficult—almost impossible—to distinguish any difference in the skin effects for these different voltages varying from 90 to 135 kv. on field sizes 0.5 to 5 cm. in diameter. It is obviously difficult to establish an absolute mathematical standard of a skin reaction for a certain size of field and intensity of radiation except within approximate limitations. The latitude of normal skin tolerance diminishes considerably with progressively larger surface areas.

Fig. 2. *A* and *B* controlled alike with 3,000 r (125 kv.). Tissue repair will occur with more rapidity in the smaller lesion *A* regardless of the difference of 10 to 15 per cent in back-scatter. The diminished tolerance of the greater surface area *B* to the same air dose is compensated by the effect of the absorption medium of the bulk of the larger growth *B*, which reduces the radiation intensity at the base of the tumor.

The shaded area (Chart II) shows a wide zone of skin reactions of an incidence and degree that are identical for a given surface area and with a variable range of radiation intensities of 250 to 650 r for fields 0.5 to 3 cm. in diameter. A faint redness usually occurs in about seven to fourteen days and is followed by a pigmentation that may persist two to four weeks (normal skin of thighs). The lower limit of the first recognizable skin change indicates the probable minimal skin effect. This would seem to be the proper threshold level and for given fields is considerably less than the corresponding maximum level. For this reason an arbitrary factor of 500 r was selected as an approximate mean level because irradiation of a superficial lesion of any size never involves more than 2 to 3 cm. width of surrounding normal skin.

Since the lesion is a neoplasm and its bulk in thickness is generally commensurate with progressive increase in size (Fig. 1) and since at no time is the "ring" or surrounding margin of healthy skin more than 1, 2 or 3 cm. in width, there is little point in multiplying factors that will only cause confusion. A dose of radiation will be tolerated by a small area, 0.5 to 5 cm., better than a similar dose given to a larger area, say 10 to 15 cm. in diameter, not only because of the increased back-scatter of 10 to 20 per cent for the larger areas, but because the tissue recovery and the defensive mechanism of repair of a traumatized area operates quicker and better for small than for large areas (Fig. 2).

Quimby, *et al.*[16] give only about 13 per cent increase in back-scatter from 5 to 100 sq. cm. fields for long wave length radiations.

There are variable reactions in different individuals to similar intensities of radiation, just as there are different degrees of skin reactions to the sun of the exposed bodies of bathers. The relatively small amount of surrounding normal skin and the bulk of tumor serving as filtration for the healthy tissue at the base of a lesion will tolerate the dosage recommended in the following plans of treatment.

TECHNIQUE

Total doses are recorded as roentgens. The skin erythema dose is arbitrarily considered as equivalent to 500 r, as before stated. This establishes a basic biologic skin unit, multiples of which will constitute the total dose of roentgens. The correlation between r and S.E.D. establishes a relative value of the dose-magnitude and gives perspective and guidance when exigencies require changes or modification. Experience with a routine procedure will lay the foundation for a methodical approach by any individual who desires to make further improvements. No change of technique is made for basal or squamous cell carcinomas.

The skin unit of 500 r (1 S.E.D.) is regarded as uniform for all surface areas of a neoplasm of 0.5 to 20 cm. in diameter, because the commensurate increased filtra-

tion value of the bulk of tumor thickness of large lesions compensates for the actual physical difference (Fig. 2). Furthermore, the width of surrounding healthy skin is not appreciably different in small and large lesions, being hardly ever more than 2 and at most 3 cm. Repair of small lesions, as already stated, proceeds better than repair of large ones.

Lead foil with aperture sufficient to include a liberal margin of normal skin (Chart III) should be used. Width of normal skin inclusion is about one-half the diameter of lesions up to 3 cm. in diameter.

Lead foil 1/64 to 1/32 inch thick must be sufficiently large to protect the treated region from stray radiation beyond the diseased part. Poorly fitting or unnecessarily large diaphragms may allow radiations to extend beyond the protecting shields to normal skin and cause serious skin reactions.

The size of the lesion is considered only as to the approximate bulk or thickness—a shallow lesion if less than 0.5 cm. elevation about the surrounding normal skin, and a large or fungating lesion if more than 0.5 cm. elevation.

Plan I. For shallow lesions less than 0.5 cm. elevation above surrounding normal skin.

Three treatments of 1,000 r (2 S.E.D.) each are given every other day. A liberal margin of surrounding skin must be included—at least 0.5, 1.0 or 1.5 cm. wide for lesions respectively 1, 3 and 5 cm. in diameter, as shown in Chart III. This determination varies with experience in estimating the extent of marginal infiltration. The radiation must extend these widths beyond any visible and palpable evidence of disease, especially beyond the marginal infiltration.

A filtration of 1 mm. Al is recommended for the second and third treatments, because routine clinical experience has shown a decidedly better skin tolerance with this shorter wave length radiation. This is an advantage and allows considerable latitude when wide margins of surrounding normal skin are irradiated. This also allows for additional treatment and even a repetition of the entire plan of treatment for possible later recurrences.

Example: 2-2-2 Technique for Shallow Lesions (less than 0.5 cm. elevation above surrounding normal skin)

Monday:	1,000 r (2 S.E.D.) 125 kv.* No filter
Wednesday:	1,100 r (2 S.E.D.) 125 kv. 1 mm. Al filter
Friday:	1,100 r (2 S.E.D.) 125 kv. 1 mm. Al filter
Total	3,200 r (6 S.E.D.) (1 S.E.D. with 1 mm. Al filter equals 550 r)

* Similar results obtainable with voltage ranges of 90 to 135 kv.

If within two to six weeks there is definitely, or a suspicion of, residual disease

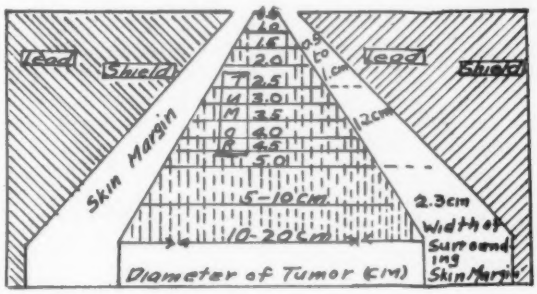

Chart III. Illustrates an estimated width of surrounding normal skin which should be included in the field of radiation according to the size of the lesion: approximately 0.5 to 1 cm. width of skin for lesions up to 2.5 cm. in diameter; 1 to 2 cm. skin margin for lesions 2.5 to 5 cm. in diameter; and 2 to 3 cm. skin margin for lesions larger than 5 cm. in diameter.

then additional treatment of 1,000 r (2 S.E.D.) is given and sharply localized to the actual or suspected residual thickening, which is usually about one-tenth to one-fourth of the original extent of involvement—with resulting complete control.

This experience illustrates that for moderately shallow lesions of any size approximately 50 per cent of the lesions will be treated in excess of the usual amount to obtain regression (Chart IV). About 2 per cent will receive inadequate treatment, but with experience one can recognize within a few weeks whether there is still residual disease. Generally such will be the case with moderately large lesions—3–5 cm. in diameter

and up to 15–20 cm. in diameter—but the residual disease is hardly more than a small proportion of the original extent of involvement, say 10 to 15 per cent. Residual disease is almost uniformly controlled by the sharp localization of an additional 1,000 r. In exceptional instances the entire original field must be treated.

It is frequently difficult to differentiate the reactions of 1,500 r as against 2,500 r,

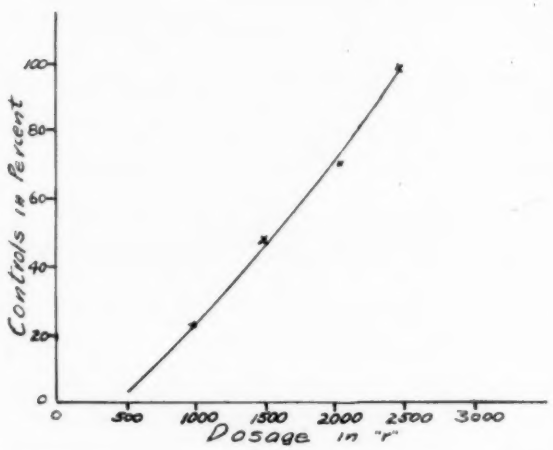

Chart iv. Symptom-free incidence by different doses (shallow lesions 0.5 cm. or less, 125 kv., 127 cases).

except for a delayed healing when the dose has been 2,500 r (5 s.e.d.). The reactions of desquamation with tendency to thick incrustations are severe. The duration varies according to the size of the lesion. For lesions 3 cm. in diameter or less, the incrustating reaction persists about a month to six weeks; for a lesion 5 cm. in diameter, about six to eight weeks. There is essentially no difference in the skin effects of the 2-2-2 (3,200 r) and the 3-3-3 (4,800 r) techniques, because of the difference in the bulk of the lesions, which act as filtrations and readily absorb the additional intensities. The marginal skin repair is not different. This is probably the result of recommending a filtration of 1 mm. Al for the second and third treatments. The additional penetration afforded with 1 mm. Al is slight, and not necessarily essential for obtaining uniformly and equally good results. Experience has shown that the important point is to include a sufficiently wide margin of healthy skin, and the filtration of 1 mm. Al clinically offers a wider margin of safety against any delayed healing, particularly if one should err in giving the 3-3-3 (4,800 r) technique for a shallow lesion. Normal tissue has been shown to tolerate very large doses with the added filtration of 1 mm. Al.

It is obvious, therefore, that no specific total dose can be formulated for residual or suspected disease, because sometimes even the entire original area of involvement must be given an additional 1,000 r (2 s.e.d.). This, however, is only occasionally necessary; that is, in but 2 to 3 per cent of patients.

Plan II. For large or fungating lesions, in excess of 0.5 cm. elevation above surrounding skin margin.

Three treatments of 1,500 r (3 s.e.d.) are given, one every other day. The inclusion of normal skin margin must be liberal (Chart iii), and the addition of filtration, 1 mm. Al, for the second and third treatment as recommended in Plan 1.

Example: 3-3-3 Technique for Large and Fungating Lesions (greater than 0.5 cm. elevation above the surrounding normal skin)

Monday:	1,500 r (3 s.e.d.)	125 kv. No filter
Wednesday:	1,650 r (3 s.e.d.)	125 kv. 1 mm. Al filter
Friday:	1,650 r (3 s.e.d.)	125 kv. 1 mm. Al filter
Total	4,800 r (9 s.e.d.)	

Additional sharply localized doses of 1,000 r (2 s.e.d.) are given to any suspected residual disease that may appear within two to six weeks or to the entire original area of involvement if necessary. Occasionally fungations are very exuberant, and as much as 8,000 r has been necessary to obtain regressions, but no precise formula can be set down for these very large lesions. Additional treatment is necessary in only about 5 per cent of average large lesions up to 10 cm. in diameter.

RATIONALE OF THE 2-2-2 (3,200 r) AND 3-3-3 (4,800 r) TECHNIQUES

Chart IV illustrates an observation on the treatment of 127 cases with different doses. All of these lesions were moderately flat, none in excess of an estimated 5 mm. elevation above the surrounding skin. The surface area ranged from 1 to 8 cm. in diameter. The types were evenly divided between basal and squamous cell carcinoma.

Only 23 per cent were controlled with 1,000 r (2 S.E.D.); 47 per cent regressed with 1,500 r (3 S.E.D.); 78 per cent disappeared with 2,000 r (4 S.E.D.); and 97 per cent were rendered symptom-free with 2,500 r (5 S.E.D.). All doses were given at one sitting. The four failures were given additional treatment of 1,000 r (2 S.E.D.) to a small residual area, 0.5 cm. diameter, and represented less than about 5 per cent of all types of lesions, of varying duration and anatomic sites. Because there are inherent factors in all cases regulating the response to irradiation, it was considered advisable to predetermine a plan of dosage that would be uniformly applicable to all lesions regardless of cellular type, size, duration and extent of involvement. Since a large area of 5 to 10 cm., even though the bulk compensates for the increased surface area, will not repair as readily as a smaller lesion, 1 to 2 cm., it was considered expedient to divide the doses.

Instead of a total dose of 2,500 r (5 S.E.D.) at one sitting, it was found that division of the treatment permitted including a large margin of apparently healthy skin, at least 0.5 to 1 cm. for lesions up to 2.5 cm. and at least 1 to 2 cm. for lesions in excess of 3 cm. in diameter. Experience soon demonstrated the tissue tolerance of the surrounding normal skin. Since the difference between success and failure is dependent on irradiation extending well beyond the visible and palpable confines of the disease, it is very essential to err, if at all, on the side of including enough healthy margin. For example, an epithelioma of 1 cm. diameter will be controlled with a single massive dose of 6,000 r sharply localized to the margins, but the risk of recurrence and even possible failure will be greater than if treatment is given over a field 2 cm. in diameter with a single massive dose of 3,000 r (Fig. 3), or better in divided doses according to Plan 1 described above. The particular advantage is the very strong evidence of an excellent recuperative marginal skin repair, as well as the fact that the divided method and dosage are consistent with uniformly good results and cosmetic effects for all sizes of moderately flat lesions.

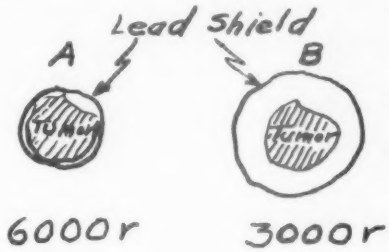

FIG. 3. *A* and *B* show same clinical results. *A*, 6,000 r (125 kv.), sharply localized; *B*, 3,000 r (125 kv.), wide skin margin treated.

The best rate of distribution of doses is difficult to establish. The plan of treatment here recommended has been established on the basis of a large number of cases over a period of ten years and has shown consistent duplication of results comparable to any that have been obtained by any other technique in our own experience or any seen elsewhere; it has permitted the management of hospital cases of extensive involvement without unduly prolonged hospitalization. The plan has been styled the 2-2-2 technique (3,200 r) of low voltage roentgen-ray (125 kv.) treatment, because it is readily understood by all members of the radiological department with a large technical service; it at once implies a fractionation of doses and all of the usual necessary precautions for protection of a large area around the field of treatment from possible stray radiation, especially if a large diaphragm opening is used to take in large lesions. It also implies precautions about fixing the part so that there will be no movement which may dislodge the lead shield or if the lead shield is fixed, that

the part will not move to such an extent that the shield overlaps a third or half or even possibly all of the lesion. Small cones only large enough to include the lesion are dangerous to use because a slight movement of the part will result in failure. Accurate measurement of distance, timing, checking of filters and fixation of head, or other part to be treated, with sand bags are also important. Constant watching of the patient will eliminate such a possibility of movement which is undoubtedly an explanation of some failures. Accurate localization and fixation, and use of the 2-2-2 technique (3,200 r), with a sufficiently wide margin, will control 97 per cent of shallow lesions without bone and cartilage involvement. The rate of treatment in this experience was considered for speed and economy. Daily treatments over a period of ten days to two weeks are burdensome, tedious and expensive. The 2-2-2 technique (3,200 r) could be advanced to treatment on three successive days, but the reaction is marked and this is easily avoided by allowing a day's intermission, or three treatments within a week.

An attempt was made to extend the treatment to one dose of 1,000 r (2 S.E.D.) per week. Very often the lesion showed complete regression at the end of two weeks, when the time was set to give the third treatment of 1,000 r (2 S.E.D.) On the other hand, this allowed sufficient time to observe a marked desquamating reaction, and on removal of the incrustation there were occasionally granulated appearances which were difficult to distinguish from possible residual disease as against irradiation reaction. As there is a possibility with lesions larger than 3 cm. in diameter of requiring additional treatment for residual disease, then this question of possible additional treatment is unduly delayed, sometimes four to six weeks, if the rate of one treatment a week is used. The resulting skin reaction for all sizes of lesions is too severe for the total of Plan I and II to be given at one sitting, especially if the recommended liberal margin of skin is included. For this reason the 2-2-2 technique (3,200 r) has been placed on a routine of three times a week—a treatment every other day.

Plan II involves a similar approach except that it was designed for fungating lesions of 0.5 cm. or more elevation above the surrounding skin margin. Fungations sometimes approach 2 to 3 cm., and very many inoperable breast cases reach proportions of 5 to 10 cm. elevation. These cases receive a dosage based on the 3-3-3 technique (4,800 r) or 1,500 r (3 S.E.D.) every other day (three times a week). After two or three weeks, if there is any question of a possible residual margin, then the routine additional dose of 1,000 r is sharply localized to the residual disease. Likewise, any recurrence even months later may be given an additional 1,000 r (2 S.E.D.) without risk of skin damage.

There is always a possibility of error with respect to estimating the size of a lesion. The dosage system is such that there will be ample tissue tolerance of a shallow lesion for the 3-3-3 technique (4,800 r) and conversely if a moderately infiltrating and fungating lesion has been underestimated as shallow and given the 2-2-2 technique (3,200 r) and at the end of a two to three week period of observation it is evident that there is still an undoubted and marked extent of disease, then an additional 2-2-2 technique (3,200 r) may be repeated without risk of hazardous effects or delayed healing. This experience is encountered occasionally at the end of three, six, and twelve months and sometimes even longer. Additional treatment by the 2-2-2 technique (3,200 r), taking in a wide margin of healthy skin, can be carried out without risk, and with expectancy of good results.

Fungating lesions may be removed with cautery and the base treated with the 2-2-2 (3,200 r) or 3-3-3 technique (4,800 r) according to the estimated extent of infiltration. This procedure is generally not satisfactory for very large lesions or in advanced age where the involvement is considerable and the patient is subjected to the shock of general anesthesia in the face

of an ultimately hopeless outlook; whereas irradiation alone will generally result in a regression comparable to a free and wide cautery dissection and in the economy of completing treatment in one week, as compared with a prolonged indeterminate hospital stay with radical surgical procedures.

High voltage (200 kv.) roentgen rays have accomplished good results in some extensive lesions, but our own experience is limited because there did not seem to be any advantage in using radiations of greater penetration.

Radium technique for shallow and small lesions involves the administration of the full dose of 5 S.E.D. at one sitting. If the lesion is infiltrating then the procedure of Plan II is carried out. The dose values in r (S.E.D.) are considered for different filtrations of 0.5 mm. Ag, 2 mm. brass, 0.5 mm. Pt, 1 mm. Pt, 2 mm. Pt, and other combinations of filters, at different distances and with varying sizes of plaques, and will be submitted in detail in a separate paper.

SUMMARY

1. There is described a technique for the treatment of cancer of the skin by low voltage roentgen rays (90–135 kv.).

2. An arbitrary factor of 500 r has been selected as a standard skin unit or skin erythema dose for the range of normal skin surfaces ordinarily included in the field of irradiation for superficial malignant neoplasms of any size rarely exceeding 2.5 cm. width of normal skin.

3. The recuperative properties of tissue repair are obviously better in small than in large areas affected by any kind of trauma, but the ultimate tissue tolerance of small and large cancers of the skin is shown clinically to be practically identical for similar intensities of long wave length radiations, because the increased back-scatter and penetration are compensated by the commensurate increased absorption properties of the progressively larger lesions.

4. The complementary factors r (S.E.D.) serve to establish some idea of the dose-magnitude in roentgens as representing so many multiples of a relative biologic indicator expressed as a skin unit or erythema skin dose.

5. A routine experience of ten years at the Philadelphia General Hospital has demonstrated an almost uniform applicability of the technique to all sizes and cellular types of lesions and that it provides a fundamental and concrete working basis from which changes may evolve to meet the exigencies of particular problems, as well as a procedure that is simple, speedy and economical.

6. The plan of treatment is designated the 2-2-2 (3,200 r) and the 3-3-3 (4,800 r) technique of low voltage roentgen treatment in cancer of the skin, according to whether the lesion is less or greater than 0.5 cm. elevation above the surrounding normal skin, regardless of the size of the surface area.

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DISCUSSION

Dr. John T. Murphy, Toledo, Ohio. Dr. Widmann, as usual, has given us a very scientific demonstration of how they treat epitheliomas of the skin in their clinic. I will have to admit that I break almost all of the rules that he has laid down this morning. We, many years ago, started treating skin cancer with small doses of radiation, and found that we had many cures but a certain definite percentage of recurrences. We now use a dose at least twice, and sometimes three times, the dose that Dr. Widman uses. The patients recover, and everyone is satisfied.

Dr. R. R. Newell, San Francisco. Dr. Widmann makes the observation that there is little apparent difference in the reaction provoked by 250 r and 650 r. We, too, have been struck by this. But there is a large difference in reaction achieved by 200 r a day and 300 r a day when carried on to marked erythema.

Dr. Widmann refuses to lower his dosage for the larger skin cancers. I would applaud him for this. However, instead of explaining that the larger tumors are usually thicker and so the base is protected from the full dosage I would insist that the base of a large tumor needs just as high a tissue dose as a small one, so that in fact the exposure needed for a large superficial cancer is even larger than what is needed for a small one.

Now I think this reveals clearly the dilemma. To cure the large cancer one needs larger dosage over a larger area, both factors increasing markedly the danger of roentgen injury to normal structures. At present we see only one solution, namely fractionation. It has become our custom to treat only the smallest skin cancers with a single exposure (3,000 r). The larger the cancer, the more we stretch out the treatment, increasing at the same time the total, according to clinical experience. We often use 1,000 r a day for four days, 800 r a day for six days, 500 r a day for two weeks or sometimes for three weeks. If biopsy shows squamous carcinoma we will usually continue to a larger total, accepting the increased danger of late damage on account of the known increased likelihood of this type to recur.

I am more and more impressed with the good rewards for fractionation in cutaneous cancer, quite as much as in deep-seated cancer.

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CLINICAL CLASSIFICATION OF CANCER OF THE CERVIX*

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THE evaluation of end-results in clinical cancer survey studies would be greatly facilitated if the method of classification employed were universal and constant in order that the greatest possible comparability between statements from different clinics could be secured. The Health Committee of the League of Nations, realizing that no such uniformity existed, has attempted to introduce a uniform classification.[1] Few collaborators from this country have adopted this arrangement of cases, prefering to invent a clinical classification of their own or confusing a previous system by modifying it.

The clinical course and history of carcinoma of the uterine cervix is now so well known and understood by all who have seriously concerned themselves with its study and treatment that a standardized and acceptable clinical classification should now be made. A standard classification should have the same exact meaning to internist, gynecologist, radiologist and statistician. Classification based on clinical extent and action offers a sound basis of approach. Methods based on treatment or results of treatment cannot offer a lasting or satisfactory basis, because methods of treatment may change radically and thereby render the system meaningless. In truth, radical changes in the method of treatment of cancer of the cervix have already occurred which now advise the disuse of former methods of classification.

In 1914, Schmitz[2] in discussing the roentgen ray in gynecology considered surgery the method of choice in the treatment of carcinoma of the uterus. He said, "I have never seen a betterment of the subjective, much less of the objective symptoms after the most careful and painstaking treatments. This fact, however, is not to be regarded as an unfortunate one, as we possess therapeutic agents in radium and mesothorium which in all probability will enable us to successfully fight this dreaded enemy of the unfortunate bearers." At this time, he classified carcinomas of the uterus as operable and inoperable and the above observations were made in treating with roentgen therapy the inoperable group. In 1916, in reporting the action of gamma rays of radium on deep-seated inoperable cancers of the pelvis, Schmitz[3] concluded:

1. The therapeutic action of radium depends on the use of a correct technique, which must be based on a careful physical examination of the patient and the physical properties and the biologic action of the metal. 2. The use of massive Roentgen rays, according to multiple field and crossfire methods in conjunction with radium therapy to destroy metastases, is an imperative necessity. 3. Certain surgical procedures must be used in radium therapy to assist the action and facilitate the application of the rays. 4. The action of Gamma rays on cancer tissues is specific and suggests positive proof of the possibility of destroying malignant tumors by the application of radium. 5. The results of radium therapy in inoperable and recurrent cancers surpass those of any other known therapeutic agent. 6. The prophylactic use of radium rays in inoperable carcinomata increases the percentage of operability and probably the efficiency of the operative procedure.

Now, surgery is seldom concerned in the therapeusis of cervical cancer. Hence, it now should be inconsistent to call a cancer of the cervix operable, borderline or inoperable. Moreover, the inconsistency is exaggerated if the clinical results are reported in terms of surgical attack if it is true that surgical removal is only an occa-

* From the Mercy Hospital Institute of Radiation Therapy, Mercy Hospital, Loyola University Clinics, Chicago. Read at the Twenty-fifth Annual Meeting, American Radium Society, New York City, June 10–11, 1940.

sional method of therapy. It is evident that classification, based on amenability to definite types of therapy, should be discontinued because the method of treatment may change at any time.

The clinical history and course of carcinoma of the cervix offers a method of classification which is apt to be influenced little by extraneous factors. Such a system is founded upon the clinical extent of the disease process. In 1920, Schmitz[4] devised a system of clinical classification for carcinoma of the uterine cervix based on its clinical extent. Later in referring to this grouping, he states,[5] "We can hope for improvement in cancer cure statistics only by instituting measures resulting in an earlier recognition and immediate proper treatment of these carcinomata." This system has been followed consistently ever since for the study, treatment and statistical reporting of this disease in our clinic. During this period, no alteration of its original design has been necessary or undertaken. It is practical, easy to comprehend and apt to be adhered to once embraced. It is offered here, at this time, not because it is new but because of its practical adaptability as a standard basis for clinical classification. Further, its use provides an aid in the selection of proper treatment and indicates the probable prognosis.

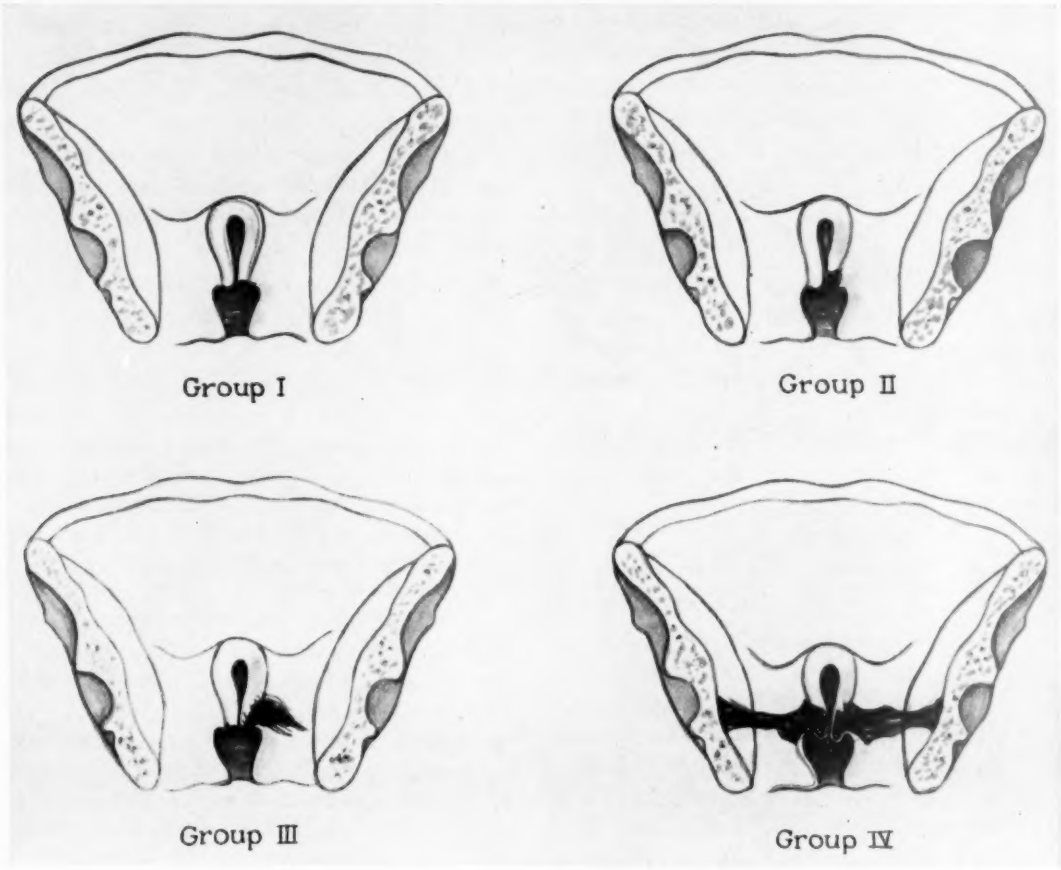

FIG. 1

It is of interest to note that at the time he devised this system of classification, Schmitz considered surgical extirpation the curative method and radiation therapy only as an adjunct and palliative procedure. With the advent of improved irradiation technique, this position was completely reversed. This reversal in therapy

necessitated no change in his clinical groupings. Moreover, the College of Surgeons uses and advocates the adoption of a classification identical with the method offered here. They make no attempt to classify according to operability. The macroscopic development of a cervical carcinoma may be considered under three stages: the nodular, the ulcerative and the necrotic stages. They may be observed in three locations: the vaginal portion of the cervix, the cervical mucosa and the endocervix.

Carcinoma of the vaginal surface of the cervix has a tendency to spread by contiguity to the neighboring mucosa of the vaginal vault and to the mucosa of the cervical canal. Carcinoma of the cervical canal may grow to the external surface or it may penetrate the walls of the cervix and invade the cellular tissues between the layers of the broad ligament. However, both types may extend in both directions and usually do as the disease progresses.

Cancer spread occurs not only by contiguity on the surface and through the walls into surrounding structures but also by emboli through the lymphatics into the regional lymph nodes of the pelvis by way of the broad and uterosacral ligament lymphatics. In long standing disease, extension to glands outside of the pelvis does occur. Only seldom are metastases transported to distant organs by blood or lymphatic streams.

The beginning cervical cancer may be a small non-ulcerated nodule impossible to diagnose by inspection, palpation or the use of colposcope or iodine stain. Its similarity to benign nodules is so pronounced that excision and microscopic inspection are necessary to determine its true nature. These nodules usually bleed readily if punctured or abraded and thereby may arouse suspicion of cancer. Histological examination of non-ulcerated nodules of the cervix will reveal and bring to early diagnosis unsuspected early cancers.

Usually the cancer nodule soon loses its surface epithelium and becomes a small ulcer. The ulceration results from death of the superficial cells which have been deprived of their nutrition by pressure of the actively growing nodule and by loss of their blood supply. The ulcer is usually deep and excavated with ragged, moth-eaten edges. The ulcerated surface is red, granular. It bleeds easily if manipulated and bleeding is usually arterial in type. A further development of the ulcerative stage is heralded by central necrosis and death of tissue. Secondary infection, no doubt, takes an important rôle in this phase. At this time, sloughing occurs and foul odor is evident.

Dependent upon the manner in which the cells grow in the early tumor, the established cancer becomes either an infiltrative or proliferating type. The infiltrative type grows inward from the vaginal focus pushing and invading the structures before it. The proliferative type is produced by the cells growing outward in papillary folds producing an everted bulky mass.

An ulcerative type is produced when either the papillary or infiltrative type breaks down and sloughs large masses of cancer tissue. Loss of blood supply, plus infection, produces this effect. Stenosis or plugging of the cervical canal by tumor, plus infection, often leads to pyometria.

As the cancer grows, the cervix and contiguous, as well as distant, structures become invaded by this disease. When an established cancer of the cervix is presented for examination and determination of the stage and extent of the process, the following questions must be asked: 1. Is the disease still confined to the cervix? 2. Has any infiltration occurred beyond the cervix into adjoining structures or does doubt exist as to its absolute localization? 3. Are the parametria, the adjacent organs, or the regional lymph nodes involved and are the invaded structures (*a*) movable or (*b*) fixed? 4. Have metastases occurred in distant organs? The disease may be said to be confined to the cervix if normal mobility of the cervix exists. A normal movable uterus may be displaced until the cervix

appears at the vaginal outlet without using undue force or causing the patient distress. A lesion less than 1.5 cm. in diameter is probably localized to the cervix. Does doubt exist as to the absolute localization of the disease to the cervix or has beginning invasion of tissues beyond the cervix itself begun? As soon as the cancer breaks beyond the limits of the cervix, the paracervical tissues become doughy and the bifurcation of the common iliac artery if the patient is relaxed by anesthesia.

Have metastases occurred to distant organs? Metastases to distant organs are discovered by careful history and physical examination. When these questions can be answered, a basis exists upon which the disease can be divided into four stages of advancement (Fig. 1).

Group I—The clearly localized growth.

CORRELATION OF THE CLINICAL SIGNS

Group	Macroscopic Appearance	Grouping of the Extent of Growth	Symptoms	Treatment
I	Nodule	Clearly localized growth in cervix. Normal movable cervix	None	Irradiation
II	Ulcer or papilloma	Doubtfully localized impeded mobility of uterus	Leukorrhea. Contact bleeding	Irradiation
III	Large ulcer or cauliflower growth with necrosis	Invasion of parametria or regional lymph nodes. Entire mass is movable.	Hemorrhage Discharge	Irradiation
IV	Crater	1. Frozen pelvis with absolute fixation of tumor. 2. Local dissemination to vagina, bladder or rectum. 3. Distant metastases.	Hemorrhage Discharge Pain	Irradiation

normal excursions of the cervix cannot be produced. Shortening of its supporting tissues restricts its descent.

Are the parametria, the adjacent organs, or the regional lymph nodes involved and are the invaded structures movable or fixed? These questions must be answered by recto-abdominal palpation, cystoscopy and proctoscopy. Bullous edema of the posterior wall of the bladder indicates the involvement of the vesico-uterine or vesico-vaginal septum by cancer. Thickening, infiltration and loss of mobility and elasticity of the anterior rectal wall and irregularity and edema of the rectal mucosa as elicited by rectal palpation and visualized through the proctoscope indicates extension of cancer into the rectal walls. The hypogastric and iliac lymph nodes can be palpated through the rectum at the

Group II—The doubtfully localized growth with impeded mobility of the uterus.

Group III—Invasion of parametria or regional lymph nodes. The entire tumor mass is movable.

Group IV—(1) Frozen pelvis with absolute fixation of tumor. (2) Local dissemination to vagina, bladder or rectum. (3) Distant metastases.

The extent or growth development is determined by general physical and special pelvic examination. The later comprises inspection by vaginal speculum and endoscopes, bimanual vagino-abdominal and recto-abdominal palpation, instrumental palpation with sound or curette and roentgen diagnostic procedures. Thereby the location and size of the growth, the condition of the parametria and adjacent or-

gans, such as vagina, bladder, rectum, bony pelvis, as well as regional gland and distant metastases, are ascertained.

A carcinoma in Group I would then be entirely confined to the cervix. It would measure from a minute, non-ulcerated nodule, just macroscopic in size, up to 1.5 cm. in diameter. The nodule should be movable within the cervical wall. The entire uterus possesses normal consistency, elasticity and mobility.

A carcinoma in Group II would spread to one-half or beyond in the cervical wall. It is surrounded by an area of inflammatory reaction which encloses dendritic processes of invading cancer tissues. The area is reddened, edematous and of dough-like consistency. Mobility of the uterus is impeded due to loss of elasticity of tissue, especially of the paracervical connective tissue.

A carcinoma in Group III would reveal extension of the cancer process in one or both parametria, or to the vesicovaginal or rectovaginal septum. The mass of cancer is as yet not fixed to the parietal pelvic fascia or bone. It is still possible to demonstrate mobility of the tissues invaded by cancer.

A carcinoma is considered to be in Group IV stage of development when the cancer process extends and invades the lateral pelvic wall, so that now the tissues on both sides are frozen or fixed. Direct invasion of the bladder, rectum or distant metastases indicates Group IV stage of development.

Heyman[1] in discussing the League of Nations' Classification states:

> Another disadvantage accompanying this device for assessing comparability is that the arbitrary rules adopted for allotting cases to the various stages are interpreted by different clinicians in a different way, thereby defeating still more the effect to assess the comparability of the samples. Consequently, a certain lack of comparability is attached to the cure rates for different stages.

This difficulty, we believe, is due to the complexity of the grouping they are advocating. If we abolish the clearly localized nodule or ulcer as the first group, are we not discouraging routine health examinations which should be carried on to discover cancer in its incipiency? The general practitioner to whom the patient first presents herself prides himself on being able to diagnose the disease when still in this stage which, at present, embraces too few of the total number of cases. (How futile is all our propaganda for early diagnosis if we are going to include moderately advanced carcinomas in our earliest stage. We will soon discourage the careful examination of the cervix and the use of other accepted means used to find the incipient cancer.) The terminal group should likewise include that stage of the disease which we recognize as the palliative group. Although improvement in irradiation technique now offers more than palliation in some of these cases we must recognize that fixation and extension to adjacent structures definitely interferes with the success of all known treatments. To recognize extension of the disease from the cervix into the surrounding parametrial tissues is not difficult. The direction of extension is of little importance but immediately places the disease in Group III. No doubt exists in the mind of the examining physician as to the progress of the disease beyond the cervix. Although previous inflammatory disease with resultant adhesions may impede the mobility of the uterus, this fact is uncovered in a careful history and if kept in mind will not make difficult the placing of cases in the second group.

Adoption of this grouping by all clinics and clinicians would greatly improve the statistics now appearing in the literature. The evaluation of different forms of treatment for all stages would be greatly simplified. By simply gathering the published statements, one could quickly determine the survival rate in this dreaded malady.

We believe that the American Radium Society by supporting the adoption of this clinical grouping for the reporting of cases of its members would influence its universal

adoption and thereby greatly improve the value of cancer statistics.

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DISCUSSION

Dr. Henry J. Ullmann, Santa Barbara, Calif. I was very much impressed with the clarity of this classification. Of course, I have known it through my friendship with Dr. Henry Schmitz but there are two points I would like clarified. I hope that Dr. Healy will discuss the second one, also.

The first stage which was referred to as nodular—does that include the superficial erosion without a nodule? We see patients with a small single patch of about a centimeter in diameter which appears as what I call a sandpaper type of erosion and which is returned carcinoma on biopsy.

We may see the entire cervix eroded, which may be reported either carcinoma or only a cervicitis. If cervicitis, multiple biopsies at different points over the cervix must be taken. Even then it may still be only a cervicitis but these are unusual.

I have seen cases in which there was no nodule and nothing abnormal whatever palpable, and yet a small eroded area is positive on biopsy. If such cases are to be included in the nodular group, it would clarify this classification very much, at least in my mind.

The other question is, should we re-classify patients after preliminary irradiation by the roentgen ray?

We know that in breasts clinical Stage II sometimes turns out to be a pathological Stage I because the axillary nodes are not malignant. We have seen cervical cases in which there was a distinct loss of mobility and even in some instances almost a fixation and yet half way through the preliminary course of roentgen treatment mobility returned to a large degree and the infiltration was reduced at least 50 per cent.

I cannot believe that such rapid regression could be a shrinkage of the carcinoma in such a short time, and I interpret the infiltration as an inflammatory reaction which has been rapidly reduced by the irradiation. Our preliminary report in that case would be a Stage III. Should that be reduced to a Stage II for our final report?

Dr. William P. Healy, New York City. I have always been impressed by the late Dr. Henry Schmitz's classification, especially of the early case. The League of Nations' classification as you know, represents in its Group I or so-called early cases any lesion that involves the cervix but does not change its size in the gross or show any evidence of spreading to the adjoining vaginal or parametrial tissues. Therefore it is, for practical purposes, a non-enlarged movable cervix but may be ulcerated or nodular.

It was my impression that Dr. Schmitz's Group I or Group A always represented a relatively small superficial ulcerative lesion, possibly not over a centimeter in diameter, and I felt that the League of Nations might subdivide their Group I in the same way to a simple, small ulcerative lesion that would be regarded as very early and call it Group I-a and then Group I-b where the entire cervix may be involved but not enlarged.

Now if we take Dr. Schmitz's classification as presented today and compare it with the League of Nations' classification, the difference will not be in the Group I cases at all.

In Dr. Schmitz's classification Group II and Group III really correspond to Group II in the League of Nations' classification. The cancer has left the cervix, is in the adjoining vaginal fornices or parametrial tissues but the uterus is still movable.

If I report a series of cases from Dr. Schmitz's classification, I will have a high percentage of cures in his Group I, possibly 75 per cent; I will have a high percentage of cures in his Group II, higher in each than I can report for the League of Nations' classification because the League of Nations' Group I will include much larger lesions than Dr. Schmitz's classification.

The League of Nations' Group II will include his Group II and Group III cases. Therefore, they cannot be compared statistically.

I think that the weakness in Dr. Schmitz's classification is in his Group IV. In the League of Nations' classification that is a so-called palliative group and it should be palliative. There should be no anticipation of cures in that group, but certainly in Dr. Schmitz's classification you can run up to 10 or 15 per cent of cures in Group IV because he includes curable cases in it.

So personally, I am for the League of Nations' classification but would like to subdivide Group I with extremely early lesions, hardly more than a superficial ulcer which may give 75 or 80 per cent of five year cures. I think that Group IV in the Schmitz classification is so inclusive of many dissimilar conditions it isn't as clear, as the League of Nations' classification. They are both good classifications, however.

Dr. H. H. Bowing, Rochester, Minn. We have always enjoyed and profited by the papers presented by the late Dr. Henry Schmitz, so it is not difficult for me to discuss his son's contribution.

It is a very tedious procedure to classify carcinoma of the cervix uteri. For example, aside from the various conditions mentioned, may I add the possibility of secondary malignant involvement of the cervix or regional vaginal walls, in which primary carcinoma of the ovary may involve the structures mentioned and in many ways simulate primary cervical carcinoma. The prognosis alone varies greatly between a Stage I carcinoma of the cervix and a Stage IV carcinoma of the ovary; however, the cervical lesion may be limited in both instances to the cervix. The differential diagnosis may be very difficult to make; clinically, it may be impossible to be certain regarding the true status of the pelvic structures. A careful history, bimanual pelvic examination, inspection, biopsy and opinions of the clinician and surgeon, as well as repeated observations during the course of treatment, all will be necessary before the diagnosis can be reasonably established.

We are all agreed with the essayists as to the importance of a classification of carcinoma of the cervix uteri. A classification suitable for universal acceptance should be simple in outline; that is, easily understood by all physicians and especially so in view of the fact that the examining physician who first sees the patient is in a good position to judge the initial extent of the carcinomatous process. Briefly stated: Stage I lesions should be limited in extent to the cervix uteri; Stage II lesions should show only moderate extension; Stage III lesions have extended well beyond the primary site and have limited mobility; usually, fixation is present; Stage IV lesions indicate what is called a "frozen" pelvis or metastasis elsewhere. It is not difficult to distinguish between the Stage I and Stage IV groups of lesions. The chief difficulty is to distinguish a Stage II and Stage III involvement. The condition may require considerable study before a true evaluation can be made regarding the site of the primary lesion and the stage of involvement.

Dr. Ullmann's question is very important and I am reminded of the method we employ at the Clinic. Patients who have had some treatment before they are seen on the radium service at the Mayo Clinic are placed in a separate group in which the lesions are known as the "modified group." The method of staging is based on the extent of the residual activity encountered. If the active lesion is very small, the lesion is classed as in the "Stage I modified" group. If the active process is extensive or if a "frozen" pelvis is noted, the lesion is classified as "Stage IV modified." The Stages II and III are between these two extremes. It should be noted that the word "stage" does not conform in meaning to the histopathologist's word "grade."

Finally, these considerations are worthy of our best thoughts. I am of the opinion that in all cases the lesions ultimately should be staged by those experienced in this particular field. If the patient has received any previous treatment which might have altered the gross appearance of the pathologic picture, then the lesions of such a patient should be classified in the separate ("modified") group which I have tried to define in the preceding paragraph.

The method of staging should be simply expressed if it is to be widely accepted. Today it is not an easy matter to arrive at a true evaluation of our observations in a determination of the extent of the malignant process. It may require much study and repeated observation before the proper stage can be determined.

Dr. Ralph E. Myers, Oklahoma City, Okla. I enjoyed Dr. Schmitz's paper very much but I would like to ask the question if he really intends always to limit the pain to Group IV. In my experience (according to his charts, he limited pain to Group IV), I have had quite a few cases in which the pain left very quickly after roentgen irradiation—four days, perhaps

—and it seems to me that we are probably dealing with some cases in which perhaps we have enlarged lymph nodes due to infection pressing on nerves rather than that they are involved with carcinoma. I just don't believe pain leaves so quickly if there is carcinoma involving lymph nodes. I think probably we get pain in his Group III rather than waiting until the case becomes Group IV. At least I have always felt that way.

Dr. Schmitz (closing). I wish to express my thanks to the discussants. I will answer the question of Dr. Ullmann first. Our Group I is either an ulcerative or nodular lesion, as I described it, and also includes the positive biopsy that is obtained from an apparently benign lesion. After all, 35 per cent of our Group I cases are microscopically diagnosed because we routinely biopsy every lesion we see.

As to re-classification, I think that it is necessary, and that is also the opinion of the League of Nations' classification. If we have fixation and classify the case as a Group IV and then it becomes movable within a week after external therapy has begun, that was undoubtedly a Group III case and we should re-classify it as such.

In answer to Dr. Healy, the League of Nations' Group II, I believe, does away with one valuable point. In postgraduate teaching—for instance, in the Graduate School of the County Hospital in Chicago where I have charge of the tumor clinic—we impress these students from around the country with the very limited extent of a Group I case, they go home looking for those lesions and are biopsying early ulceration, chronic cervicitis and by this means are discovering carcinoma in its incipiency. If we teach them that Group I may invade the entire cervix, as long as it is localized to the cervix they are not going to look for the early lesion. I can't agree with what you say about the weakness of Group IV in our classification. After all, if you have complete fixation and that fixation wasn't inflammatory or if you have invasion of the bladder, or invasion of the rectum, you may have some palliative relief for a year or two but that certainly is a hopeless group of cases.

I don't agree with Dr. Bowing that the classification of cases is difficult. I am convinced that we can recognize the minute the disease begins to leave the cervix. If you find, on rectovaginal palpation, edema either in the paracervical area or any of the surrounding parametrial tissues, even though that is inflammatory, we cannot say that carcinoma cells haven't gone out into the lymphatics, and that places the case in Group III.

Pain does not occur until fixation takes place or pyometra or pressure on the ureter are present. These are the three complications that cause pain in carcinoma of the cervix. If it responds to a very short course of radiation therapy, it was probably inflammatory fixation, the inflammatory reaction regresses and the case should be re-classified as Group III

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THE TREATMENT OF CARCINOMA OF THE OVARY*

IMPROVEMENT OF RESULTS WITH POSTOPERATIVE RADIOTHERAPY

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SUCCESSFUL treatment of ovarian carcinoma has always been a difficult problem. The cure rate with surgery alone is generally conceded to be uniformly low. Our findings and the studies of other investigators appear to indicate that postoperative radiotherapy effects a noteworthy improvement in the therapeutic results. As the disease is not extremely common,[8] the number of cases in the reported statistical studies is comparatively small. We are therefore presenting a review of the literature and 124 additional cases treated by surgery alone or by surgery plus radiation therapy.

Table I shows the low operability rate and high primary operative mortality in a combined series of cases.[2,4,13,16,17,18,19,21,23,24,25,26,27,30,32,33,34] The presence of ascites and widespread disease has been found to increase the risk considerably.[19]

TABLE I

OPERABILITY AND PRIMARY OPERATIVE MORTALITY

	Total Number of Cases	Percentage
Operable*	643	36.9
Operative mortality	over 200	15.1

*"Operable" cases are those in which all apparent neoplastic tissue is removed.

It is universally agreed that the determinant and most important factor in the efficacy of therapy is the extent of metastases. The failure to classify the cases according to stage of progression has made evaluation of the early reports difficult.

The material has been grouped most frequently into stages of progression regardless of histological type. The classification which we have employed groups the cases into four stages:

Stage I: Primary tumor unilateral and completely removable, no visible metastases.

Stage II: Local metastases present, but completely removable with primary tumor so that no visible disease remains.

Stage III: Local metastases present, but only partially removable with primary tumor.

Stage IV: Cases with advanced carcinomatosis peritonei in which only exploratory celiotomy or removal of large tumor masses may be performed as diagnostic and palliative measures.

Since no division was made between Stage I and Stage II in the majority of statistical surveys these stages will be considered as one group in Table II, i.e., completely removable tumors.[4,9,13,27,28,30,31,33] It is evident from the table that the supplementary use of radiation therapy does not significantly alter the five year survival rate in completely removable ovarian carcinomata. However, to compare the prognosis of a combined series of Stages I and II cases treated by surgery alone with a similar series which received postoperative irradiation may be misleading. Our studies agree with reports of other investigators that surgery alone gives results comparable to surgery plus postoperative irradiation in Stage I. In Stage II, however, postoperative radiotherapy definitely improves the results.[2,4,27]

The value of postoperative radiation therapy in those cases of ovarian carcinoma where part of the disease remains following surgery (Stage III) is also presented in Table II.[9,13,16,20,21,27,28,30,31,33] The increased

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TABLE II

FIVE YEAR SURVIVALS
Review of Literature

Stage of Progression	Treated by Surgery Alone		Treated by Surgery and Postoperative Irradiation	
	Total No. of Cases	Survival Rate	Total No. of Cases	Survival Rate
I and II	104	48.5%	165	50.3%
III	94	6.4%	166	21.1%
IV	—*	Rare*	150	6.0%

* Although a large number of individual cases in this group has been reported, no statistical analysis of the material has been found recorded.

number of five year survivals in the irradiated group appears to be of statistical significance.

In cases with extensive abdominal metastases (Stage IV) the prognosis is universally considered as extremely grave. The five year survivals treated by surgery alone have been so few in number that no statistical analysis of these cases has been found.

Many individual case reports have appeared wherein radiation therapy has resulted in marked palliation of apparently hopeless and moribund cases of ovarian carcinoma with widespread disease.[4,6,9,11,14,15,29] These instances, although interesting, are not of statistical value. However, in a combined series of various investigators, 150 cases of Stage IV ovarian carcinoma were treated by postoperative radiotherapy.[9,13,16,20,21,27,28,30,31,33] Of these, 9 patients (6 per cent) survived five years. We believe this result represents a distinct improvement over the non-irradiated group.

The radiation employed by the different investigators varied considerably. The range of voltage varied from 100 to 200 kv. In the vast majority of cases the dosage given by the various investigators was inadequate according to present standards. It was noteworthy that the results with postoperative radiotherapy reported before 1930 approached those reported after that year only in Stage I cases where radiation does not seem to play an important rôle. However, in the Stage II and III cases the results were much better after 1930. Undoubtedly, this was due to increased dosage and improved methods of administration. Montgomery and Farrell[21] found that of 5 cases of Stage II ovarian carcinoma which received intensive therapy 3 survived five years. In 4 instances where the radiation dosage was small all were dead by the fifth year. Jacobs and Stenstrom[15] reported 50 patients with ovarian carcinoma who received what they considered adequate postoperative therapy. Of these, 16 (32 per cent) survived five years. In 9 cases the dosage was considered grossly inadequate. None of these patients lived five years. The implications for adequate therapy in all cases seem clear from the foregoing.

From 1928 to 1935, 153 cases of carcinoma of the ovary were admitted to the private and ward services of The Mount Sinai Hospital. Of these, 124 were followed for one year or longer, and form the basis for this study. The remaining 29 cases were not seen following operation and are therefore not included.

The diagnosis was confirmed in each case by histological study. In 15 instances this was obtained by paracentesis or biopsy of an inguinal node. In 31 cases exploratory laparotomy was performed, and in the other 78 some form of extirpative surgery was done. Thus, 78, or 62.9 per cent, were considered operable. It must be remembered that the operable group thus defined included instances in which visible metastases were left in the abdomen even after removal of the major part of the

growth. If only those cases in which complete removal of all the gross disease could be accomplished were considered operable, the operability rate declines to 39.5 per cent. This is comparable to the results reported by other investigators.

There were 15 postoperative deaths, a primary operative mortality of 9.8 per cent. The procedures performed on these patients were: panhysterectomy 2; supravaginal hysterectomy and bilateral salpingo-oöphorectomy 3; oöphorectomy 3; exploratory laparotomy 5, and paracentesis 2. Three of these cases were in Stage I. In 6 patients metastases had occurred, and in the remaining 6 the disease was hopelessly advanced with carcinomatosis peritonei present. It thus appears that surgical intervention in ovarian carcinoma was accompanied by a high primary operative mortality in our cases also.

Our material was divided into four large groups according to the type of treatment: surgery alone; surgery plus inadequate roentgen irradiation; indeterminate roentgen irradiation, and adequate roentgen therapy. Each large group was then further subdivided into four subgroups according to the stage of progression. These stages were described above.

In reviewing the radiation therapy given to the cases, we found a great variation in the amount and type of treatment employed. Therapy was classified as "adequate" in this study only if a minimum of 1,200 r (in air without backscatter) was delivered to each of three pelvic fields in approximately one month. The factors used were 180–200 kv., 0.5 to 2.0 mm. copper filtration and target-skin distances of 50 to 70 cm. Many of the patients had two such courses within one year. Others had one series of treatments in which a total of 2,000 r was delivered to each of four portals in a period of six weeks. Where quantitative and quality factors were less than those described above therapy was considered inadequate.

Ten patients received radiotherapy outside the hospital. In these instances the exact radiation dosage could not be obtained. These are listed under indeterminate roentgen therapy.

The inadequacy of surgery alone in the treatment of carcinoma can readily be seen from Table III. Only patients with Stage I disease have a reasonably good prognosis with surgery alone. If the 3 postoperative deaths are excluded from the 7 patients in this group, then 3 of the remaining 4 sur-

TABLE III

FIVE YEAR SURVIVALS WITH SURGERY ALONE

	No. of Cases	Alive				
		1 yr.	2 yr.	3 yr.	4 yr.	5 yr.
Stage I	7	3#	3	3	3	3 (42.9%)
Stage II	12	9*	6*	4*	2	1*** (8.3%)† (11.1%)
Stage III	13	3	2	2	0	0
Stage IV	31	0	0	0	0	0
Totals	63	15*	11*	9*	5	4*** (6.3%) (6.7%)

Three patients died postoperatively.
* Each asterisk represents one case which was alive and well in the year recorded but was not followed thereafter.
† Where there are 2 percentages listed, the upper indicates the absolute survival rate and the lower represents the corrected rate (non-followed cases omitted).

TABLE IV

FIVE YEAR SURVIVALS WITH OPERATION PLUS INADEQUATE ROENTGEN THERAPY

	No. of Cases	Alive				
		1 yr.	2 yr.	3 yr.	4 yr.	5 yr.
Stage I	5	4	2	2*	1	1* (20%)† (25%)
Stage II	5	4	3*	2	2	1* (20%) (25%)
Stage III	3	2	0	0	0	0
Stage IV	7	0	0	0	0	0
Totals	20	10	5*	4*	3	2** (10%) (11.2%)

* Each asterisk represents one case which was alive and well in the year recorded but was not followed thereafter.

† Where there are two percentages listed, the upper indicates the absolute survival rate and the lower represents the corrected rate (non-followed cases omitted).

vived five years and longer. However, the number of cases is so small that no conclusions can be drawn. Table IV presents those patients treated by surgery plus 'inadequate" postoperative irradiation. This group may be added to the series treated by surgery alone because the amount of radiation administered was minimal. In this series, of 5 Stage I cases only one survived five years. Thus, of 12 localized unilateral cases treated principally by surgery only 4 survived five years.

A comparison of cases in Stages II and III shows that for practical purposes whether visible metastases are apparently completely removed or not the five year survival rate is the same. This observation is of considerable importance to the pelvic surgeon. Where metastases are difficult to remove without compromising important structures such as bowel, bladder or ureter, it would be better to depend on postoperative radiotherapy rather than attempt surgical ablation.

TABLE V

FIVE YEAR SURVIVALS WITH OPERATION PLUS INDETERMINATE ROENTGEN THERAPY

	No. of Cases	Alive				
		1 yr.	2 yr.	3 yr.	4 yr.	5 yr.
Stage I	3	1	1	1	1	1 (33.3)
Stage II	2	2	1	1	1	1 (50%)
Stage III	4	4	1	1	1	1 (25%)
Stage IV	1	1	0	0	0	0
Totals	10	8	3	3	3	3 (30%)

Despite the fact that 63 cases were treated by surgery alone, there was a relatively large number of inoperable cases, and the prognosis was extremely poor. Only 4 cases, or 6.3 per cent, survived for five years. In addition, the life expectancy in this group was extremely short. Seventy-six per cent died within the first year.

When Table IV is compared to Table III it is immediately seen that the results with inadequate irradiation and without roentgen therapy are similar.

cases are alive for a similar period. This is true regardless of the stage of progression of the disease, and most clearly demonstrated in the advanced cases. A comparison of cases in Stage III demonstrates the effectiveness of radiotherapy in retarding tumor growth. Whereas the 13 untreated cases are dead within four years, of 11 treated patients 5 survived the fourth year.

If we may be permitted to assume that the number of five year survivals is an index of the value of radiotherapy, then a

TABLE VI

FIVE YEAR SURVIVALS WITH OPERATION PLUS ADEQUATE ROENTGEN THERAPY

	No. of Cases	Alive				
		1 yr.	2 yr.	3 yr.	4 yr.	5 yr.
Stage I	10	10*	9*	8**	5	5**** (50%)† (90.0%)
Stage II	5	5	3	2	1	1 (20%)
Stage III	11	8	7	6	5	2 (22.2%)
Stage IV	5	4	2	1	1	1 (20%)
Totals	31	27*	21*	17**	12	9**** (29.0%) (33.3%)

* Each asterisk represents one case which was alive and well in the year recorded but was not followed thereafter.

† Where there are two percentages listed, the upper indicates the absolute survival rate and the lower represents the corrected rate (non-followed cases omitted).

Table V shows the results in those cases which had indeterminate amounts of radiotherapy. Slight improvement in life expectancy becomes apparent. However, the small number of cases detracts from the statistical value of the series.

A comparison between cases treated by surgery alone (Table III) and those receiving adequate postoperative roentgen therapy (Table VI) is striking. The improved life expectancy and increased number of five year survivals are probably significant. Whereas, 27 irradiated cases (87 per cent) among 31 are alive at the end of one year, only 15 (23.8 per cent) of 63 non-irradiated

study of Tables V and VI seems to indicate that radiotherapy does arrest the disease as well as prolong life. In 63 cases treated by surgery alone only 4 are alive after five years. If the 15 postoperative deaths are removed from this series then 4 cases (8.3 per cent) out of 48 are alive for this period. In comparison, the irradiated cases show an absolute five year survival rate of 9 (29 per cent) of 31 cases. We believe these results to be significant.

The prognostic value of morphological classification and histological grading of malignancy was also investigated. Our material included 8 cases of pseudomucinous

cystadenocarcinoma, 3 dermoid cysts associated with carcinoma, 3 dysgerminomas and 3 granulosa cell carcinomas.

Of the 8 patients with pseudomucinous cystadenocarcinoma 5 had large cysts without evidence of metastases. One did not receive roentgen therapy and only the neogenic ovary was removed. She is alive and well seven years postoperatively. Three of the others received roentgen therapy following removal of the neogenic ovary. Two are well for three and one for seven years respectively. The fifth patient had a supravaginal hysterectomy and bilateral salpingo-oöphorectomy followed by roentgen therapy. She died two years later of intestinal obstruction and metastatic carcinoma of the intestines. Of the remaining 3, one died immediately following operation. The second had bloody ascites without visible metastases. Only the neogenic ovary was removed and no roentgen therapy was given. She died one year postoperatively. The other had gross metastases with bilateral disease. A panhysterectomy was performed and adequate roentgen radiation administered. She succumbed to the disease one and a half years later. From the above small number of cases it appears that the behavior of pseudomucinous cystadenocarcinoma is similar to that of serous cystadenocarcinoma and medullary carcinoma.

The 3 cases of carcinoma of the ovary associated with dermoid cysts were also found to behave similar to the other ovarian carcinomata.

Evidence indicates[22] that certain carcinomata, i.e., dysgerminoma and granulosa cell carcinoma, may offer a better prognosis than the other more frequently encountered forms of primary malignant neoplasms of the ovary. In our material there were 3 cases of dysgerminoma. They are well four, five and seven years respectively. In 2 there were no metastases. Roentgen radiation was used in treating only one of these patients. The third had a chain of enlarged preaortic glands which reached to the diaphragm. She received intensive roentgen therapy and despite the probable lymph node metastases is alive and well after four years. Of the 3 patients with granulosa cell carcinoma, one died postoperatively. The other 2 patients are well six and eight years respectively. Both received adequate amounts of roentgen radiation. The disease was localized in one case; the other was Stage II.

Seventy-three of the tumors were histologically graded according to the degree of malignancy by Dr. Paul Klemperer. The following criteria were employed: (1) proliferative tendency of the glandular epithelium; (2) cell uniformity, and (3) number of mitotic figures. The tumors were divided into two groups: those of high and those of low malignancy. Sixty (82.2 per cent) of these 73 neoplasms were highly malignant. Table VII illustrates the relationship between extent of metastases clinically and degree of malignancy histologically. As would be expected, it is apparent that

Table VII

STAGE OF PROGRESSION AND DEGREE OF MALIGNANCY HISTOLOGICALLY

Histological Grading	Total No. of Cases	Stages I	II	III	IV
Low malignancy*	13	4	5	1	3
High malignancy†	60	8	12	6	34
Percentage of cases of high grade malignancy	82.1	66.7	80.6	85.7	91.9

* Histologically classified as Grades 1 and 2.
† Histologically clasified as Grades 3 and 4.

among the more advanced cases there is a greater proportion of highly malignant neoplasms.

Because of the small number of cases of low malignancy it was impossible to obtain a statistically significant comparison of the results with surgery alone and with surgery plus postoperative irradiation in the high and low malignancy groups. However, our impression is that histological grading plays a definite but minor rôle in prognosis. The practical value of histological grading appears further limited by the observation that a large proportion (82 per cent) of the growths are highly malignant. It would appear, therefore, that the clinical stage of progression of the disease is the major factor in prognosis and determination of type of therapy to be employed.

Surgery alone has been repeatedly shown to be most effective in the localized, unilateral cases. Where the neoplasm has extended beyond one ovary, surgery appears inadequate to cope with the disease. Even in the Stage II cases where the local metastases can apparently be removed, only 11 per cent survive five years.

The value of postoperative radiotherapy is apparent in all reported series. Its relative importance and effectiveness increases proportionately with the stage of progression of the neoplasm. Thus, its benefits are least apparent in Stage I, while in Stage IV it is the most beneficial form of treatment.

Radiotherapy to be effective must be given in adequate amounts. The failure of inadequate radiotherapy to improve the results over surgery alone is clearly demonstrated in the reports of Montgomery and Farrel,[21] Jacobs and Stenstrom,[15] and in our series of cases. In Stage IV maximal mounts of radiation have not been given by some radiologists because the patient was considered too ill to tolerate such treatment. Our studies seem to indicate that such an attitude may be unwarranted. There is usually no prolongation of life, no noteworthy relief of symptoms and no possibility of a five year survival with small, "palliative" quantities of radiation. An attempt wherever feasible should be made to give all patients the benefit of maximum dosage. Frequently repeated blood transfusions, parenteral administration of liver extract, vitamin B_1, high caloric feedings, oral barbiturates, and the use of a face mask to de-ionize the air[5] are of value in combatting radiation sickness and improving the general condition of the patient. Ascites, if present, should be removed. With such therapy significant prolongation of life occurs in a number of apparently hopeless cases and an occasional five year survival may be expected.

Despite adequate, postoperative radiation therapy, the ultimate prognosis remains poor where the disease has progressed to Stage IV. In addition, the primary operative mortality in the advanced stages is extremely high even though only exploratory laparotomy is performed. For these reasons it would appear logical to attempt a slightly different approach to the therapy of this type of case. We feel that if by clinical examination and the presence of tumor cells in the ascitic fluid, the diagnosis is clear beyond reasonable doubt, intensive preoperative radiation therapy should be employed first. This may be followed, when feasible, by surgical extirpation. In this manner the extent of the metastatic disease can occasionally be greatly diminished and the general condition of the patient improved. Operative mortality may thus be significantly reduced and the number of five year survivals increased. We have not employed this method as yet. However, encouraging results have been reported from its use by others.[10]

There is no unanimity at present as to what constitutes adequate dosage. We believe that a dose closely approximating normal tissue tolerance should be delivered during one course of treatment. This method appears preferable to a number of small courses given over a period of a year or longer. The following physical factors were employed by us: 180–200 kv., 0.5 to 2.0 mm. copper or equivalent filtration and 50–80 cm. target skin distance. Six portals

of entry are usually available; two anterior pelvic, two gluteal and two ischial. The latter average 10×10 cm. in size, while the remaining fields are approximately 10×15 cm.; 200 r (in air without backscatter) is usually given to each of two fields daily, and the portals are treated in rotation. The average near-tolerance dose is 2,000 to 2,500 r per field when treated in the above manner for a period of one to one and a half months. The treatment should be individualized. Variation in mode of administration and dosage will depend on general radiation tolerance, local variations of the disease and upon the configuration of the pelvis. The total dose is usually conditioned by the reactions of the skin, bladder, rectum and hematopoietic system. The patients must be examined frequently during the course of therapy. If metastatic disease is found in the upper abdomen, this region should be subjected to the maximum tolerated dosage. This is distinctly less than the pelvic dose because of the comparative radiosensitivity of the upper abdominal viscera.

With the aid of shock-proof therapy equipment additional and perhaps valuable portals are available. These are right and left vaginal vault. The use of these additional fields may be worthy of trial, particularly where cul-de-sac and paracervical metastases are present or when intravaginal radium cannot be employed. Comprehensive reports of postoperative radiation therapy in ovarian carcinoma with voltages above 200 kv. have as yet not appeared. Supervoltage radiation was not used in our series. Whether the five year cure will be increased by adequate dosage of extremely hard radiation can only be determined by clinical trial.

A significant feature apparent from the analysis of our series is that the number of five year survivals is practically identical in Stage II and Stage III cases treated with surgery alone. This number is extremely small. In the great majority of these cases panhysterectomy was performed. The removal of the uterus did not influence the prognosis. Since the effectiveness of radiotherapy depends in great measure upon the dosage administered, it would appear advisable, at least theoretically, to allow the uterus to remain and thus permit the use of intrauterine radium therapy. In this manner an equivalent of 3 threshold erythema doses could be administered to an area whose borders are 5 cm. from the centrally placed radium source in all directions.[1] This form of therapy has been repeatedly advocated by Heyman[12] Schroeder,[30] and Schmitz.[29] The results reported by these investigators are encouraging. In a similar manner, the presence of cul-de-sac recurrences or deposits would at least theoretically indicate the use of vaginal radium.

SUMMARY

1. A clinical classification of ovarian carcinoma according to stage of progression is presented, and the necessity for its use in evaluating therapeutic results stressed.

2. A critical analysis of reports of other investigators whose cases were amenable to classification is made.

3. Our material consists of 124 cases of ovarian carcinoma which are reviewed with particular reference to therapeutic results.

4. The primary operative mortality was 9.8 per cent.

5. Sixty-three patients with ovarian carcinoma were treated by surgery alone. Of these, 4, or 6.3 per cent, survived five years.

6. Sixty-one cases were treated by surgery plus postoperative radiotherapy. Thirty-one patients received moderately large amounts of radiation (considered as "adequate" in this series) and 7 (29 per cent) were alive five years. Twenty received "inadequate" radiation dosage and 2 (10 per cent) survived five years.

7. The major factor in prognosis and determination of type of therapy to be employed is the clinical stage of progression of disease. Morphological classification and histological grading appear to be of minor importance.

8. Maximal dosage of radiation therapy should be employed whenever possible.

Small, "palliative" amounts play a minor rôle in the treatment of ovarian carcinoma.

9. The rationale for permitting a normal uterus to remain in situ and employing it as a radium carrier in order to increase the intrapelvic dose is discussed.

10. The administration of radiation therapy preoperatively in Stage IV cases of proved carcinoma is advocated.

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THE RELIEF OF SYMPTOMS IN RAYNAUD'S DISEASE BY ROENTGEN THERAPY

REPORT OF CASE

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THE condition now known as Raynaud's disease was first described by Brodie[3] in 1837, but because of the more extensive writings of Raynaud[6] in 1862, this entity now bears his name. He fully described the malady and set forth the following diagnostic criteria. These are: (1) intermittent attacks of changes of color in the acral parts (hands, feet, chin, tips of nose, ears); (2) symmetrical or bilateral involvement; (3) absence of clinical evidence of occlusive lesions of the peripheral arteries, and (4) gangrene or trophic changes, if present, limited mainly to the skin. To these four criteria, Allen and Brown[1] have added the following to further differentiate the condition: (5) the disease must have been present for a minimal period of two years, and (6) there must be no evidence of disease to which it could be secondary.

The etiology of this condition is still not definitely established. Formerly it was believed that the disease was limited entirely to females; more recent statistics indicate that this is true to the extent of 90 per cent of the cases. Syphilis has been mentioned as being causative in the older literature, but the condition cannot be considered as true Raynaud's disease when lues is present.

The onset of the symptoms occurs mainly in the thirties, with the forties next, and then the twenties. Nationality, marital status, and occupation have no bearing on this condition. The complications of this malady are scleroderma, gangrene, recurrent infections and arthritis. Jones[5] noted a similarity between "rheumatoid arthritis" and Raynaud's disease.

Most therapeutic agents are of little benefit in this condition. Heat, warm socks, arsenic, thyroid extracts, atropine and many other drugs have been suggested but have not been successful. Operations on the sympathetic nervous system have been advised by Adson and Brown[2] as the best method of treatment and have been considered curative in the uncomplicated cases. Roentgen therapy has been tried by the same group of observers, with but indifferent results. The therapeutic result obtained in the following case is at variance with the findings of these authors:

REPORT OF CASE

A white woman, aged forty-one, came to the clinic four years ago because of attacks of numbness and blanching of her fingers during cold weather. Further questioning revealed the fact that the same symptoms, but not so marked, had been noted in the toes. She also had noted that with a sudden drop in room temperature, her fingers became quite cold. She stated that during cold weather slight ulcerations appeared at the tips of the fingers of her right hand; these disappeared during warmer weather.

Physical examination revealed that the skin of the hands and feet was of normal color and texture. The radial, dorsalis pedis, and posterior tibial pulses were of good quality. On the distal end of the right index finger, there was a cornified area which was tender to touch. There was a slight cornification of the distal part of the left index finger, but this was less painful than on the right side. On immersion of the hands in cold water, there was prompt blanching. As they became warmer, the skin first assumed a slightly bluish-red color, following which the normal color reappeared. A similar reaction was noted when she held a glass of ice water.

The general physical examination was nega-

* Service of H. Milch, M.D.

tive. Routine urine examination, as well as special tests for determining the presence of arsenic[4] in the urine, was also negative. Lues was excluded by history, physical and neurological examinations, and serological tests.

In 1936, hydrotherapy in the form of contrast baths to the extremities was given without any improvement. Early in 1937 she was given several injections of sodium thiosulphate, without any improvement. Injections of muscle extract did not help her condition. From December, 1937, to April, 1938, she received eleven intermediate voltage roentgen treatments over the cervical and lumbar areas totaling 1,200 r. During all this time she did not have any pain or ulcers. In October, 1938, the patient visited the clinic and reported that although she had been comfortable for the past six months, she was again experiencing mild attacks of blanching of the fingers with pain due to the cold weather. She received roentgen therapy from October through February, 1939, and during these winter months she again became symptom-free.*

SUMMARY

A case of Raynaud's disease is presented in which characteristic symptoms and signs were noted during four successive winters. Initial employment of the ordinary therapeutic measures failed to result in improvement. Subsequently, roentgen radiation to the cervical and lumbar regions gave considerable symptomatic relief for two consecutive winters.

* The roentgen treatments were given by the Department of Roentgenology of the Hospital for Joint Diseases: Dr. M. M. Pomeranz, Director.

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THE EFFECT OF HIGH VOLTAGE ROENTGEN RAYS ON THE HEART OF ADULT RATS

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INTRODUCTION AND REVIEW OF PERTINENT LITERATURE

THIS study was undertaken because there is some doubt concerning the effect of high voltage roentgen rays on the heart when this organ is irradiated. Not infrequently this question arises in the treatment of neoplastic disease of the mediastinum and of the lung adjacent to the heart, and of the left breast. The internist in the cancer institute and those internists closely associated with tumor clinics in general hospitals must particularly understand these effects in order to recognize and treat irradiation and post-irradiation complications more intelligently.

Warren and Whipple[7] were unable to demonstrate any clinical or organic changes in the hearts of animals that were irradiated over the thorax and abdomen. Gordon, Strong and Emery,[4] in working with rabbits that received large single or smaller multiple doses of roentgen rays, were unable to find any constant cardiac changes. In some animals there were occasional areas of fatty infiltration or necrosis which they felt may have been due to toxic or nutritional effects. Davis[1] irradiated the entire thorax or hemithorax of dogs and rabbits. Three of the dogs showed thickening of the right auricle and pericardial petechial hemorrhages. Similar changes were not found in the left auricle. Histologically these changes were hyalinization and necrosis of the right auricular muscle. No changes in the ventricular muscles were noted. Hartman, Bolliger, Doub and Smith[5] irradiated dogs and sheep through the precordium. The doses varied from 8 to 18 S.E.D. All of the sheep died within thirty days with pericardial effusion without pericarditis. The hearts were distended two to three times normal size. The right side of the heart was especially enlarged. Histologically there were indistinct striations, irregular staining and moderate infiltration of round and wandering cells. Some of the dogs showed similar myocardial changes, plus beginning fibrosis and thickening of the coronary vessels, and narrowing of the lumen. They concluded that irradiating the heart caused definite myocardial damage. Warthin and Pohle[8] irradiated rats and rabbits through the precordium. The average dose was in the neighborhood of 660 roentgens. A few of the animals received two, three and four times this dose. The animals were then killed at frequent intervals. The histologic findings were frequent occurrence of Zenker's necrosis and some fatty changes in the myocardium. They concluded that the Zenker's necrosis may have been due to the method of fixation and the fatty change could be explained on a nutritional basis. Domagk[3] noted immediate myocardial changes in animals that received irradiation to the entire body. He found that myocardial fibrosis did occur in the surviving animals. Warthin and Pohle[9] continued their work on rabbits and rats. This time they used divided doses of high voltage roentgen rays through a precordial portal, giving 660, 300 and 300 r at monthly intervals. The animals were killed at intervals varying from eight to thirty-two days following the last treatment. They found either Zenker's necrosis or fatty changes or both in all the hearts. All had severe bronchitis or bronchopneumonia. Unfortunately, many of the control animals had similar pulmonary changes and some showed evidence of Zenker's necrosis in the myocardium. They believed that the pulmonary changes were secondary to the irradiation and the control animals developed pulmonitis as a result of contact with the infected animals.

Desjardins[2] made a very extensive review of the literature up to 1932 and concluded that all of the work up to that time was inconclusive concerning the effect of irradiating the heart. He concluded that any permanent cardiac damage resulting from irradiation could only result from extremely large doses such as were never used clinically.

When one considers the varying reports of different investigators it seemed that there might be room for argument concerning the effect of irradiating the heart. Therefore we undertook to determine if these myocardial changes were produced; and if they were, what is the critical dose and the mechanism of the histologic changes.

EXPERIMENTAL

As a preliminary study, we determined the dose of roentgen radiation that could be tolerated by the animal when delivered in a single exposure to the entire body. Young, healthy, adult male and female albino rats, 2.5 to 3.5 months old were used in this study. Their weight ranged from 120 to 200 grams at the time of irradiation. The animals were firmly fixed to a stiff pasteboard by means of adhesive tape and remained so during the time that the radiation was delivered. Each animal was then placed under the roentgen tube and doses of 150, 300, 500, 700, 850, 1,000 and 1,250 roentgens were given.

The following factors were used: 200 kv., 30 ma., a filter of 0.5 mm. Cu and 1.6 mm. Al and 50 cm. target-skin distance. The intensity of radiation was 56 r/min.

This study included a total of 25 rats. The results showed that all of the animals survived a dose of 300 r or less. A dose of 500 r killed all of the animals, seven, within eighteen days, the shortest time interval between irradiation and death being two days. With a dose of 700 r one animal died on the sixth and one of the seventh day. A dose of 850 r or more had a markedly harmful effect on the nutrition of the animals. They all died two to five days after irradiation. We concluded that a dose of about 400 r is the border line between lethal and sublethal when it is given to the entire body.

The experimental procedure for irradiating the precordium of the rats was the same as outlined previously except that a specially constructed shield of lead 4 mm. thick with 1 mm. of celluloid attached was used. This shield had a portal cut into it measuring 1 by 1.5 cm. This was placed over the animal after it had been firmly fixed to the pasteboard so that the portal was directly over the heart, the location of which had previously been determined by palpation. In this way all of the animal except the precordial area was protected from the roentgen rays (Fig. 1). The source of radiation was a standard water-cooled Coolidge roentgen tube with the following factors: 200 kv., 30 ma., a filter of 0.5 mm. Cu and 1.6 mm. Al. At 45 cm. target-skin distance the intensity was 69 r/min; at 31 cm. the intensity was 146 r/min. In a few instances

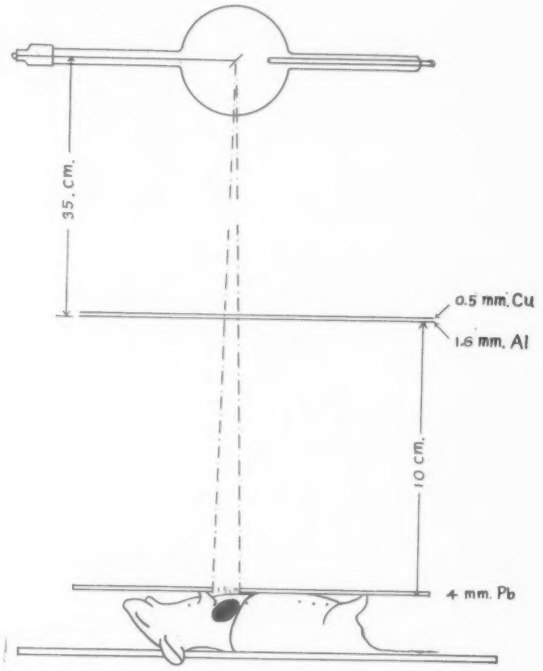

Fig. 1. Diagram showing the position of the heart of a rat during irradiation, with respect to the heart, diaphragm, filters and source of radiation.

where extremely large doses were given, unfiltered roentgen rays were used at an intensity of 337 r/min.

A record of each animal was made, including the general physical condition, its weight at frequent intervals, and the duration of life following treatment, until death or until the animal was sacrificed. At the end of definite intervals the animals

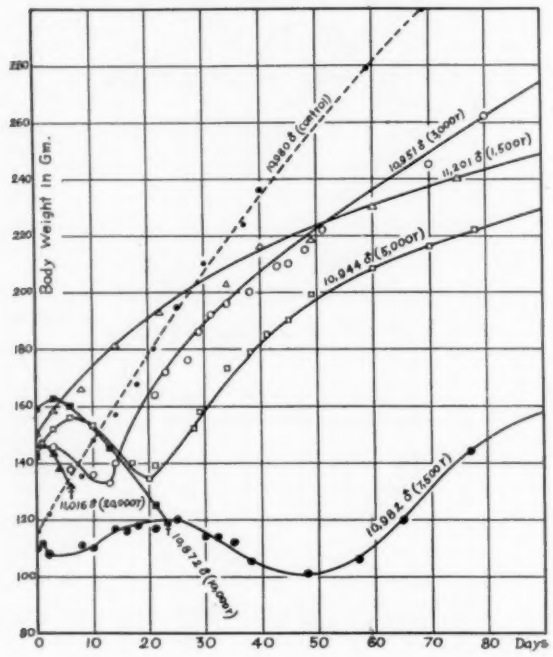

Fig. 2. Curves showing the growth of young adult rats after receiving different doses of roentgen rays on the heart. The broken line indicates the growth curve of a normal non-irradiated rat.

were killed with ether. An autopsy was done on each animal immediately and macroscopic changes were noted. Sections of the heart, lung, liver and occasionally spleen were fixed in formalin, cut and stained with hematoxylin and eosin. In a few instances the tissues were fixed and stained for glycogen and fat. The hearts were sectioned transversely so that cross sections of the right and left ventricles and interventricular septum were obtained at different levels.

The rats all received large single doses of 1,500, 3,000, 5,000, 7,500, 10,000 and 20,000 r. Control rats were kept in each cage with the animals.

Using this source of radiation and factors in the above animals, the computed depth dose reaching the anterior cardiac wall was 90 per cent and the posterior wall 75 per cent. The skin erythema dose for the human subject is 750 r, measured in air. In animals, however, one can only determine the degree of epilation that occurs. The skin does not develop the characteristic redness at doses less than 1,500 r when epilation begins.

Effect on Nutrition and Weight of the Animals

When one irradiates the heart in the living animals under these conditions, the anterior and posterior mediastinal structures necessarily receive almost as much radiation as the heart itself. It is also impossible to avoid irradiating the adjacent lung and particularly that portion of the left lower lobe lying immediately posterior to the heart. A smaller portal than 1 by 1.5 cm. would minimize the damage, but then the accuracy of hitting the heart would be endangered since it is impossible to immobilize absolutely the conscious animal on the pasteboard.

We sought to determine just how much effect irradiation had on the general well being of the animals by keeping close watch on their general health and weight (Fig. 2). Up to and including doses of 5,000 r, there was no constant appreciable effect on the weight and health of the animal. All acted normally throughout the duration of the experimental procedure and had normal growth rates. At 7,500 r 5 rats maintained their weight. One died in twenty-four days. The remaining 6 animals gained weight but more slowly than the animals receiving 5,000 r or less. Of the animals receiving 10,000 r over the precordium 3 lost weight slowly and died on the twenty-third, twenty-sixth, and seventy-first day. Three maintained their body weight and the remaining one gained weight slowly at first and then gained weight at a normal rate.

The 20,000 r animals lost weight steadily from the start and died at varying intervals of from six to fourteen days after irradiation.

Ten animals received 3,000 r, 5,000 r, 10,000 r, 20,000 r, and 25,000 r over the right lobe of the liver. The 5,000 r rat gained weight normally. The 10,000 r and the 20,000 r animals maintained weight and the 25,000 r animal died in thirteen days from hepatic and pulmonary abscess.

Five animals received similar doses over the right thigh muscles and all gained weight normally even though the 25,000 r rat had a large area of necrosis of the thigh extending down to the bone.

Those animals that received 1,500 r over the right upper lobe of the lung with the production of a diffuse bronchopneumonia either maintained their weight or had normal growth curves.

In summary, up to 7,500 r there is little or no appreciable effect on the growth of the animals. At 10,000 r 3 lost weight while the remaining 3 maintained weight and one gained weight slowly. At 20,000 r weight loss began immediately. Irradiating the liver, thigh or lung alone has little effect on the weight. These latter animals all looked healthy when killed.

EFFECT ON THE SKIN

The following reactions were produced on the skin: 750 r produced no epilation. At 1,500 r partial epilation occurred at the third week and this was followed by a gradual return of the hair. No vesiculation occurred. Doses of 3,000 r, 5,000 r, and 7,500 r produced gradual increase in the completeness of the epilation, temporary at lower doses and permanent at higher doses. Only mild vesiculation resulted but no skin infection followed. At 10,000 r complete epilation occurred, together with a variable degree of ulceration which became superficially infected and was followed by crusting. At 20,000 r none of the animals survived long enough to permit the full extent of the reaction over the precordium to develop. In the animals receiving 25,000 r over the thigh and liver a large area of necrosis resulted beginning about the third week.

THE EFFECT OF 1,500 r ON THE HEART

Three animals received 1,500 r of filtered high voltage roentgen rays over the precordium in single doses, as previously outlined in the section on technique. They were killed on the seventh, fourteenth, and twenty-first day, respectively, after irradiation. Grossly the hearts were all normal. The lungs showed small pinpoint area of subpleural hemorrhage in those portions of the right and left lung that were superjacent and subjacent to the heart. In all, these were few in number. In the rats killed on the fourteenth and twenty-first day after irradiation, these areas had become indistinct and paler as though they were being absorbed. The abdominal viscera were all grossly normal.

Microscopically the pericardium, myocardium, endocardium and coronary vessels showed no abnormalities. The lungs showed some engorgement of the vessels, especially the capillaries, and an occasional area of subpleural hemorrhage. The pleura itself showed no area of exudation, and the pleural endothelium was intact.

THE EFFECT OF 3,000 r ON THE HEART

Five rats received 3,000 r over the precordial area in single doses of filtered high voltage roentgen rays. They were killed on the seventh, fourteenth, twenty-first, twenty-third, and thirty-fourth day, respectively, after irradiation. Two of the animals maintained their weight and the remaining 3 had normal growth curves. All were in good health at the time they were sacrificed.

Grossly the pericardiums of all the rats were normal. Two of the rats had slightly flabby myocardiums; the remaining three were of normal consistence. There were similar pinpoint subpleural hemorrhages in the lung immediately adjacent to the heart. The remaining lungs were grossly

normal except in one animal in which there was moderate diffuse pulmonary congestion. There was no evidence of pleural exudate or increased pleural fluid. The abdominal viscera in all animals were normal.

Microscopically the hearts were all normal. In some there were areas of mild capillary congestion but this may have been due to the anesthesia. The lungs in all 5 animals showed varying degrees of bronchopneumonia. There was congestion and thickening of the alveolar septa, diffuse round cell infiltration and areas of alveolar exudate.

EFFECT OF 5,000 r ON THE HEART

Five rats received 5,000 r in single doses of filtered high voltage roentgen rays over the precordium. They were killed on the seventh, fourteenth, twenty-first, twenty-third and sixty-eighth day respectively after irradiation. Three of the animals had normal growth rates. One did not gain for seventeen days and then had a normal growth curve. One, killed on the seventh day, did not gain.

In these animals the pericardiums were grossly normal. The myocardiums in 4 animals were slightly flabby. In the animal killed on the sixty-eighth day the myocardium was normal. The lungs of these animals showed more advanced changes in that portion of the left lobe underlying the heart. They were mottled with small scattered areas of congestion. There was no evidence of pleural reaction.

Microscopically the pericardium, myocardium, and endocardium of all the animals were normal. The muscle fibers of the animal killed sixty-eight days after irradiation stained unevenly, some fibers stained deeply but were not hyalinized. The coronary vessels were slightly dilated but the vessel walls were unchanged. The sections of the lungs subjacent to the heart showed varying degrees of bronchopneumonia, some quite severe and others relatively mild. Other sections away from the cardiac area showed mild inflammatory changes. No pleural reactions were present.

EFFECT OF 7,500 r ON THE HEART

Ten rats received 7,500 r of filtered high voltage roentgen rays over the precordium in one single dose. They were killed on the seventh, eighth, fourteenth, sixteenth, nineteenth, twenty-eighth, twenty-ninth, thirty-first and eightieth day respectively One died on the twenty-fourth day. Five of the animals gained weight, the remaining 5 maintained their weight.

Grossly the hearts were all slightly flabby and darker than normal but were otherwise not remarkable. The pericardium of all animals was grossly normal. The lungs in all the animals were congested from a slight to a marked degree. No pleural reactions were present. In the animal that died on the twenty-fourth day the pulmonary congestion was especially marked. The abdominal viscera were all grossly normal. In the animal killed on the thirty-first day there was infarction of the upper fourth of the lower left lobe.

Microscopically the hearts did not present any unusual changes except in 2 animals. In the heart of the animal killed on the nineteenth day there was a fairly large area of localized round cell infiltration in the wall of the left ventricle. The cells were all lymphocytes. The surrounding muscle fibers were perfectly normal. In this animal there was a severe pneumonitis in the lower left lobe of the lung. In the animal killed on the eightieth day the muscle fibers stained irregularly. The cross striations were not well marked. Some fibers stained deeply but were not hyalinized. There were no areas of round cell infiltration. The coronary vessels in this animal showed a mild degree of thickening of the wall.

Sections of the lungs showed moderate to severe pneumonitis. In some animals the changes in the left lower lobe resembled abscess formation with complete disappearance of normal lung structure.

Sections of the livers of the animals showed no constant changes. Some were normal and some showed very slight de-

grees of congestion of the central vein which could very well have been the result of the anesthesia.

EFFECT OF 10,000 r ON THE HEART

Eight animals received 10,000 r in single doses of high voltage roentgen rays. Three of the animals were treated with unfiltered roentgen rays. The remaining 5 had the usual filter. One animal died on the twenty-third day, one on the twenty-sixth day and one on the seventy-first day. These animals lost weight from the beginning. The remaining animals either maintained their weight or gained weight slowly after irradiation and were in good health when killed. They were killed on the eighth, fourteenth, twenty-third, twenty-ninth and seventy-third day, respectively, after irradiation.

Grossly the animals that lived presented a normal pericardium; the myocardium was usually dark and somewhat flabby. The left lower lobe of the lung posterior to the heart showed marked congestion and occasionally some hemorrhage. The remaining portion of the lung was slightly redder than normal. None had increased pleural fluid or pericardial fluid.

The animal that died on the twenty-third day had a small pericardial effusion, a left pleural effusion and a right hemothorax. The lungs were congested throughout. The animal that died on the twenty-sixth day had a small pericardial effusion and bilateral pleural effusion (Figs. 3 and 4). There was some hemorrhage in the left lower lobe. The animal that died on the seventy-first day was destroyed through error and no gross examination was possible.

Sections of the heart of the surviving animals showed normal pericardium and endocardium. The muscle cells stained well, nuclei appeared normal and there was no intercellular edema. In some there were occasional very small areas of round cell infiltration which were interpreted as the result of pulmonary changes. The blood vessels were not remarkable. The lungs

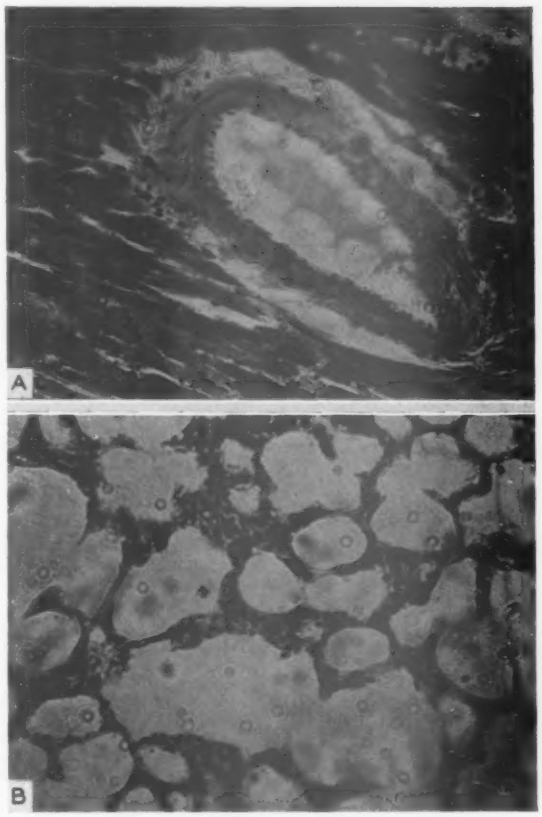

Fig. 3. *A*, heart of a normal rat. Note the closely packed muscle fibers. *B*, lung of a normal rat.

showed varying degrees of atelectasis and bronchopneumonia. No appreciable pleural reaction was noted.

The hearts of the animals that died showed an entirely different picture. The pericardium and endocardium were normal. The most striking feature was intercellular edema as evidenced by fibrin, marked capillary engorgement and some areas of capillary hemorrhage. There were many areas of diffuse round cell infiltration. The muscle cells in general stained well but were thinner than normal. The cross striations were well marked in some areas, poorly delineated in others. Many of the muscle nuclei in one animal showed swelling and stained poorly and were slightly to markedly pyknotic. The muscle nuclei of the other animals were normal.

The lungs of both animals showed marked passive congestion. There was no pleural

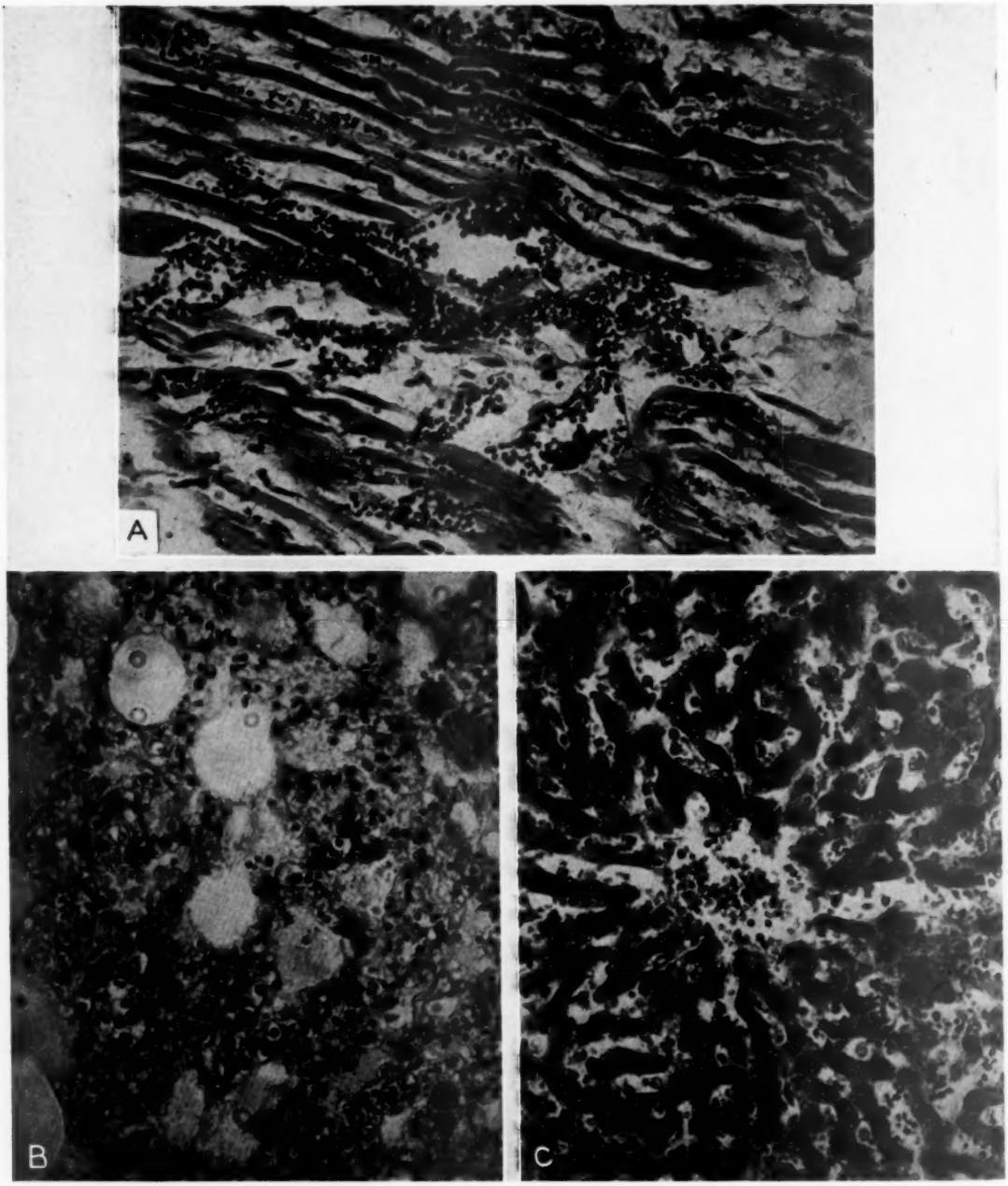

Fig. 4. *A*, heart of rat that died twenty-six days after receiving 10,000 r over the precordium. Note the engorged capillaries, intercellular edema and areas of hemorrhage. *B*, lung of same animal showing areas of pneumonitis, capillary engorgement and pulmonary edema. *C*, liver of same animal showing moderate degree of passive congestion of central vein of hepatic lobule.

reaction. The liver in one animal showed passive congestion.

That the edema and alteration in the morphology and staining of the muscle cells and nuclei were the direct result of irradiation and not secondary to pulmonary changes seemed probable, inasmuch as the animals that survived had bronchopneumonia with fairly normal hearts whereas the lungs of the animals that died showed passive congestion. The gross findings were of cardiac decompensation also.

EFFECT OF 20,000 r ON THE HEART

Five rats received 20,000 r of high voltage roentgen rays through the precordial area. In 4 cases it was given unfiltered and in one the usual filter was used. All of the animals died in from six to fourteen days. Two died on the sixth day, one on the tenth day, one on the twelfth day and one on the fifteenth day. All lost weight steadily, ate poorly and were sickly following irradiation. All died too soon for a skin radiation reaction to appear but in a few there was some subcutaneous edema over the precordial area.

Grossly one had a pericardial effusion. Two had bilateral pleural effusions and one had bilateral bloody pleural effusion. All of the animals had markedly congested lungs, in some areas it appeared hemorrhagic. All of the hearts were dark, dilated, flabby and in one animal there was gross hemorrhage in the myocardium. All of the animals showed moderate congestion of the abdominal viscera and one had a small degree of ascites.

Microscopically in 3 animals there was a mild degree of subpericardial edema and congestion with a mild degree of round cell infiltration. The pericardial endothelium was intact in all and there was no evidence of a pericardial exudate. The endocardium was normal.

The myocardium presented a distinct picture (Fig. 5). There was diffuse edema, capillary congestion and capillary hemorrhage in all. There was diffuse moderate to severe round cell infiltration. The myocardial fibers were shrunken in many instances. In other areas they stained fairly well and cross striations were well marked. The nuclei in many areas were either slightly swollen or had become pyknotic and some were undergoing dissolution. The coronary vessels were all dilated and filled with blood. The vascular endothelium appeared intact. The walls in many areas were thinned out and the vessel walls contained vacuoles. The lungs showed varying grades of bronchopneumonia, atelectasis and edema, the latter always predominating. Sections of the liver showed passive congestion.

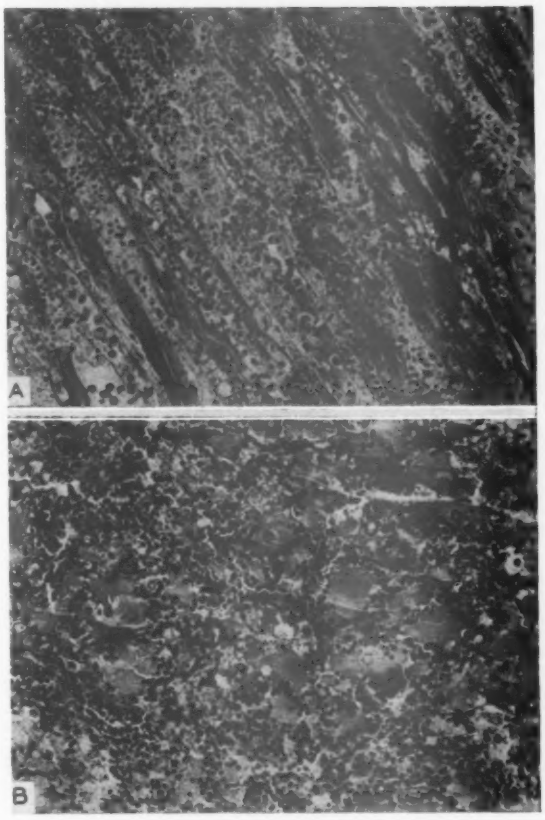

Fig. 5. *A*, heart of rat that died twelve days after receiving 20,000 r over the precordium in a single dose. Note the total destruction of many of the muscle fibers, hemorrhage and round cell infiltration. In many muscle cells the cytoplasm is apparently coagulated. Some of the muscle fibers are only hollow tubes filled with acid staining debris. *B*, lung of same animal showing pneumonitis and marked pulmonary edema.

IRRADIATION OVER THE LIVER

Five rats received high voltage roentgen radiation over the right lobe of the liver in varying single doses. Two received 5,000 r of filtered roentgen rays. One was killed twenty-six days after irradiation and one 129 days after irradiation. The first maintained its body weight and the second had a normal growth curve. One animal that received 10,000 r (filtered) over the right lobe of the liver maintained its weight and died on the twenty-eighth day. One re-

ceived 20,000 r (unfiltered), maintained its weight and died on the forty-eighth day. The last received 25,000 r of unfiltered rays, lost weight steadily and died on the thirteenth day.

Grossly the heart and pericardium were normal in the 5,000 r and 10,000 r animals. In one animal there were a few areas of pulmonary congestion. The liver and other abdominal viscera were all grossly normal except in the 25,000 r animal. In this animal the heart was flabby and the lungs were hemorrhagic in areas. The 25,000 r animal developed an abscess of the skin and underlying liver and adjacent right lung. The pericardium was normal and the heart was slightly flabby.

Microscopically one of the hearts showed an occasional small area of round cell infiltration. Otherwise the hearts were not remarkable. The muscle cells and nuclei appeared normal. The lungs showed varying degrees of bronchopneumonia, particularly marked in the 20,000 r and 25,000 r animals. In the 5,000 r animals the liver sections were normal. In the 10,000 r animals there were areas of focal necrosis in the liver and many of the remaining hepatic cells contained vacuoles and stained poorly. The nuclei were not remarkable. The 25,000 r animal showed coagulation necrosis of hepatic cells.

Effect of large single doses over the thigh

Four rats received single doses of 5,000 r, 5,000 r, 10,000 r, and 25,000 r over the inner aspect of the right thigh muscles. The same size portal was used as in irradiating the precordium. They were killed at intervals of 26 days, 129 days, 28 days and 29 days respectively, after irradiation. The 25,000 r animal received unfiltered roentgen rays; the remaining animals received the usual filtered roentgen rays through copper and aluminum.

Grossly the thigh muscles were slightly paler than normal in the 5,000 r 129 day and the 10,000 r twenty-eight day animals. The 25,000 r animal had a large necrotic ulcer in the thigh muscles. All of the animals, including the latter, were in good health at the time they were killed. The hearts and other viscera were all grossly normal.

Microscopically the hearts and lungs of all the animals were normal. The thigh muscle of the 5,000 r 129 day animal showed a moderate degree of round cell infiltration in the intermuscular septa and beginning fibrosis. The muscle cells seemed normal. The 10,000 r twenty-eight day animal showed a very slight degree of round cell infiltration but the muscle cells were unchanged. The 25,000 r animal's thigh muscle at the edge of the ulcer showed a diffuse round cell infiltration and necrosis of the muscle cells. Other cells stained fairly well, cross striations were present and the nuclei were normal.

Effect of 1,500 r over the right lung

Nine rats received 1,500 r over the right upper lobe through a portal 1 by 1.5 cm. The same factors were used. This dose can produce in rats a severe type of bronchopneumonia. Two were killed in seven days, 2 in fourteen days, 3 in twenty-one days and 2 in twenty-nine days after irradiation.

Grossly, the remarkable findings were evidence of consolidation in the right upper lobe of all the rats and varying degrees of gross congestion mild to moderate in degree in the remainder of the lungs. None had gross signs of pleurisy or excess pleural fluid. The hearts were all normal and other viscera were likewise normal.

Microscopically all the animals had varying degrees of bronchopneumonia from moderate to severe. The right upper lobe was always more severely affected than the remainder of the lung. The hearts of all the animals were within normal limits. There were no areas of round cell infiltration, the muscle cells and nuclei were normal. The pericardium, endocardium and coronary vessels were normal.

It seemed likely, on the basis of the results, that bronchopneumonia was not a

factor in producing the cardiac changes that followed irradiation of the heart directly with higher doses of roentgen rays.

EFFECT ON THE WHITE BLOOD COUNT

The total white blood count of rats taken before feeding is extremely variable. Figures are given from 9,000 to 20,000 as noted by Scarborough.[6] The cellular elements vary widely also. Polymorphonuclear leukocytes range from 10 to 45 per cent; lymphocytes from 50 to 91 per cent; eosinophiles from 0.2 to 3.5 per cent; and basophiles from 0 to 1.3 per cent.

In 5 rats the total count varied from 9,000 to 17,000. The polymorphonuclear cells varied from 5 to 18 per cent, lymphocytes from 75 to 90 per cent and eosinophiles from 1 to 2 per cent. Each of these animals received 7,500 r over the precordium in the usual manner. Two days later the white blood count in these animals ranged from 2,100 to 4,700 and there was a marked shift in the differential count. The polymorphonuclear cells had increased up to 58 to 77 per cent and there was a corresponding drop in the lymphocytes. The monocytes and eosinophiles were unaffected. The white blood count gradually rose over a period of three weeks to an average of 7,500 but had not regained the normal figures at the end of one month. The polymorphonuclear cells at this time were slowly decreasing to 40 to 50 per cent of the total count and the lymphocytes were showing a corresponding increase.

These animals were killed at varying intervals of from one to four weeks, and examined in the routine manner. The hearts were unchanged and there was the usual amount of bronchopneumonia present. Four gained weight normally and one maintained its weight. None showed any signs of toxic change in the viscera or other areas of infection in the body despite the leukopenia present. These gross, microscopic and hematological findings support the view that the rats withstand quite well the degree of bronchopneumonia produced inadvertently by our method of irradiation and that toxicity plays a very minor rôle in producing the changes noted in the hearts.

DISCUSSION

In considering the effect of irradiation on the heart, as it has been studied in the foregoing experiments, certain definite undesirable features can readily be seen. The heart of the patient receiving radiation therapy is not subjected to such massive single doses even with the million volt machine. It would be extremely difficult to repeatedly irradiate animals daily with fractionated doses. Such facilities are seldom available. Secondly, the heart is not irradiated *in toto* as frequently as only in part. That is, in lesions of the lower esophagus, certain thymic tumors and carcinomas of the lung very close to the hila and in mediastinal lymphoblastomas, the bulk of the heart receives the radiation. In lesions of the upper esophagus tumors of the medial half of the breast and certain bronchogenic carcinomas, only a portion of the heart is irradiated. Thirdly, the adjacent lung is irradiated necessarily, particularly the lower medial portion of the lower left lobe. This gives rise to the added complication of bronchopneumonia. However, since it was the purpose of the experiment to determine the amount of radiation the heart could stand these objections were foreseen and taken into consideration.

The lung changes are unavoidable unless accuracy is sacrificed by using a smaller portal. All of the animals receiving 7,500 r or more developed variable degrees of bronchopneumonia that was roughly proportional to the dose. The changes did not resemble radiation pleuropulmonitis according to Stewart. Our impression is that the changes produced in the 10,000 r and 20,000 r animals' hearts were not the result of infection because the remaining animals of the 10,000 r group presented no unusual cardiac findings, even though the degree of bronchopneumonia was just as marked. Moreover, the animals showing cardiac changes presented gross evidence of cardiac decompensation with pleural and pericar-

dial effusions and hepatic congestion. It is fair to assume that if pulmonary infection did play a part in producing these changes the 7,500 r and 10,000 r animals would have had at least some microscopic evidence of cardiac damage. With the leukopenia produced by irradiating the blood current as it passed through the heart, one would think that the infection, if it did play a part in the changes seen, would have had ample opportunity to do so.

One point in particular is worth noting; that is, the extreme resistance of the endocardium and pericardium to high voltage roentgen rays. None of the animals showed evidence of pericarditis grossly or microscopically, even when a pericardial effusion was present. In some of the 20,000 r animals there was a mild degree of subpericardial swelling with capillary engorgement and round cell infiltration, but the endothelium was intact throughout.

The results of the experiments support the conclusions of previous investigators that the myocardium is extremely resistant to high voltage roentgen rays. These animals were all vigorous healthy male and female rats. The question whether changes could more easily be produced in hearts, the seat of disease, particularly fibrosis, since these changes occur at an age when the reparative processes are not as strong as in younger individuals, cannot be answered as yet. Another question remains unanswered; that is, are there more subtle changes taking place in the myocardium that are not evident microscopically but will only appear at some later date? The frequent progressive fibrosis that occurs in the pectoral muscles following irradiation of the axilla makes one wonder whether the same changes take place in the heart late in the post-irradiation period. At present we have a group of animals that received radiation to the heart some months ago and which will be the subject of a later report.

Clinical experience suggests that very little happens to the heart during the course of treatment through the precordial area or at the height of the radiation reaction. The blood pressure tends to lower figures in some cases and the pulse sometimes accelerates. There have also been reports in the literature that variable arrhythmias occur. At first glance these changes seem to be the direct result of irradiation. Closer observation over a longer period of time usually alters this thought, and the cardiovascular changes are found to be due to some other factor: the malignant disease itself, inanition, anemia, or infection or a combination of them.

The claim has been made that roentgen irradiation of distant parts of the body may affect the heart adversely due to the circulation of toxic substances thought possibly to be split protein products. In our experiments this has not been borne out except in one exceptional instance in which the animal developed a hepatic and right pulmonary abscess.

SUMMARY AND CONCLUSIONS

1. Adult male and female rats received various doses of roentgen rays to the body as a whole and to the heart.

2. About 400 r is the lethal dose when applied to the entire body.

3. The critical dose, when the heart alone is irradiated, is 10,000 r or more in one single dose.

4. The myocardial changes thus produced are hemorrhage, round cell infiltration, myocardial degeneration and necrosis.

5. The pericardium and endocardium withstand single doses up to and including 20,000 r.

6. The bronchopneumonia inadvertently produced by the technique of irradiation plays little or no rôle in the changes observed.

7. The leukopenia produced has no apparent effect on the general health or in the production of the myocardial changes seen in these animals.

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RELATION OF SEX HORMONES TO TUMORS OF THE FEMALE REPRODUCTIVE SYSTEM*†

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INTRODUCTION

IN THIS review the words "estrogen" and "estrogenic substance" will be used to mean any of the various compounds which have powers resembling those of the female sex hormone. Included, then, are estradiol which is presumably the true human female sex hormone as produced in the ovary, estrone (theelin) and estriol (theelol) which are found in human urine and probably are excretion products. It also includes equilin and equilinene, which are found only in horse urine, and two synthetic estrogens of high potency, triphenylethylene and stilboestrol. The natural estrogens have also been used in the esterified forms, such as estrone benzoate or estradiol dipropionate.

The word "androgen" will refer to any substance having powers resembling those of the male sex hormone. Testosterone has been isolated from testes and is considered to be the true male sex hormone. Androsterone and dehydroandrosterone are androgens as found in the urine and are considered to be metabolized excretion products.

Progesterone is the progestational hormone as found in the corpus luteum. It is believed to be metabolized and excreted in the urine in the form of the biologically inactive pregnanediols.

CARCINOMA OF THE BREAST

Experimental Evidence

Mouse: Lathrop and Loeb[90,91] first established that there was a direct relationship between the ovaries and breast carcinoma in mice. They noted that some of the females, but none of the males, of the particular strain of mice that they were studying, had spontaneous breast carcinomas. Castration decreased the incidence of carcinoma and pregnancies increased this incidence. These findings were confirmed (Cori[21]) and it was found that implantation of ovaries into the normally carcinoma-free males of these strains caused carcinomas to develop (Murray,[114] de Jongh and Korteweg[77]).

Proof that estrogens were the ovarian factors influencing the incidence of breast carcinomas was educed by Lacassagne.[81,82] He increased the incidence of breast carcinomas in females and caused them to appear in males of the same strain by administration of estrogens. Many workers have subsequently confirmed these findings (Burrows and Kennaway;[18] Burrows;[17] Cramer and Horning;[23,24] Bonser;[11,12] Gardner, Smith, Allen, and Strong;[54,56] Suntzeff, Burns, Moskop, and Loeb[140]). The accumulated data have shown that the incidence of carcinomas of the breast can be increased in female mice and that carcinomas can be induced in males that come of a strain in which the females normally have spontaneous carcinomas. Breast carcinomas cannot be induced by estrogens in either male or female mice of a strain that never has spontaneous carcinomas (Suntzeff, Burns, Moskop, and Loeb;[140] Cramer and Horning;[23] Bonser;[12] Lacassagne;[86] Gardner[51]). One exception to this statement is a report by Bonser, Stickland, and Connal.[13] However, the validity of their report can be questioned in that the strain of mice (CBA) they reported as free of spontaneous carcinoma has been shown to have spontaneous carcinoma in other laboratories.

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Rats: In most laboratories, estrogens apparently have not caused breast carcinomas in rats, in spite of large dosages given over long periods of time (Emge[36,39].) Geschickter,[59] however, has produced definite breast carcinomas in male and female rats with very high dosages. He states that his strain of rats is free from spontaneous breast carcinomas. This colony of rats has been inbred and observed for five years. There is only one other partially confirmatory report on this matter. McEuen[101] obtained one breast cardinoma in a series of rats after prolonged estrogen administration.

Guinea pigs: Several workers have administered estrogens to guinea pigs for prolonged periods (Nelson;[116] Moricard and Cauchoix;[112,113] Dessau;[32] Florentin and Binder[43]). No breast carcinomas have been reported.

Rabbits: Estrogens have been given to rabbits also for long periods (Lacassagne;[84] McDonald[99]). No breast carcinomas were reported.

Monkeys: Folley and Zuckerman[47,48] have given prolonged high dosages of estrogens to monkeys. Other workers have given estrogens to this species for shorter periods of time. No carcinomatous breast changes were produced.

Clinical Inferences

Studies in the human female are of necessity limited to the correlation of numerous and widely variant clinical impressions. Many authors have reasoned that if carcinoma of the breast originates as a direct result of an endocrine disturbance, then some menstrual irregularity should be evident. Taylor[143] and others have recorded such irregularities in the patients who have carcinoma of the breast while they are still in the menstrual phase of their lives. This group comprises only one-third of all the patients with breast carcinoma (Taylor[144]). Therefore, two-thirds of all the patients have carcinoma diagnosed after cessation of menstrual function. This fact does not necessarily signify that the carcinoma developed after the menopause. It is possible that the inception of the malignancy occurred during menstrual life but failed to develop until later in life. Such a possibility, however, has not been conclusively demonstrated.

Statistics published by Lane-Claypon[89] indicate a variance with the above contention. She carefully studied 500 patients with breast carcinoma. The patients were grouped according to all possible data obtainable, such as age, parity, nationality, occupation, etc. To make the study more accurate and valuable, she chose a control group of 500 patients who had no malignancy and who had no history of a malignant tumor. These women corresponded as near as possible in all respects to the patients with breast carcinoma. Lane-Claypon's statistics show that there was more menstrual irregularity in the control group than in the group with breast carcinoma. The author did not believe this indicated the true situation since the control group was chosen from hospital and dispensary patients and therefore might be expected to have some menstrual irregularity. She was inclined to believe that more irregularity was present in the carcinoma group. It seems, however, that such a supposition is not tenable in view of the figures presented.

It is impossible, of course, to compare data obtained from animal experimentation with those obtained by studies of the human female. It is interesting, nevertheless, to note that Suntzeff, Burns, Moskop, and Loeb[139] reported no increased irregularity of the estrus cycle in the mice of high spontaneous carcinoma strains as compared with the cycles in mice who had few or no spontaneous breast carcinoma. Thus, on the basis of clinical reports, it is not established that menstrual irregularities denoting endocrine disturbances are associated with carcinoma of the breast in any increased incidence.

It has been suggested that the simultaneous occurrence of breast carcinoma and pelvic tumors indicates the importance of

some endocrine factor as a common etiological cause. Taylor[145] stated that the most common combination of tumors is carcinoma of the breast and carcinoma of the endometrium. He believed this strongly suggested a common endocrine cause since the breast and the endometrium are two of the tissues most profoundly influenced by estrogens. On the other hand, however, it should be recalled that the vaginal epithelium, which is even more readily and profoundly altered, is rarely the site of malignant change. Schreiner and Wehr[134] reported 18 instances of carcinoma of the breast and carcinoma of the genital organs that were observed in a series of 307 cases of multiple tumors. Four of the genital lesions were carcinoma of the endometrium and 4 were carcinoma of the cervix. This report suggests a mere casual association of genital and breast tumors. Meigs,[106] in reporting a series of 250 multiple malignant tumors, found a group of 14 carcinomas of the cervix in which 9 were associated with carcinoma of the breast. Associated with 7 malignant tumors of the uterine body, he found 3 carcinomas of the breast. In 11 instances the tumors seemingly appeared spontaneously. He concluded that these facts indicated some association between the various regions where malignancies develop.

Although many findings suggest some common endocrine etiological cause for development of breast carcinoma, no absolute clinical proof has yet established this fact.

It is generally accepted clinically that carcinoma of the breast progresses rapidly in the presence of a pregnancy. It has been suggested that the rapid growth is associated with the marked increase of hormone concentration in the body at that time. Trout[149] reported 15 patients in whom one breast was removed for carcinoma and who later became pregnant. Thirteen of these developed carcinoma in the remaining breast and 12 died promptly.

The view that the higher concentration of estrogens during pregnancy is important in development of breast carcinoma cannot be completely accepted since there are numerous works that indicate carcinoma of the breast is more common in nulliparous than in multiparous women (Lane-Claypon[89]). Cohn[20] found that the Negro had as much or more breast carcinoma than the white race, and yet had fewer pregnancies. He believed that pregnancy per se was not an essential factor in predisposing to carcinoma. Abnormalities of lactation subsequent to pregnancy he thought were more important as a contributing factor. Adair[1] observed frequent lactation deficiencies in patients with breast carcinoma. Lane-Claypon,[89] however, failed to find any such lactation disturbance. She also considered unilateral lactation and found no correlation between lactation abnormalities and breast carcinoma development. There is as yet no conclusive proof of association between lactation deficiency and breast carcinoma. Trout[150] suggested that obstruction and irritation of breast tissue resulting from abnormal lactation might be important in the production of carcinoma.

The importance of estrogenic substances has been intimated by inference from studies of patients with carcinoma of the breast who have been castrated. Herrell[67] noted a low incidence of breast carcinoma in patients who had been castrated. He suggested that this indicated that the ovarian hormones (estrogens) favor carcinoma by preventing epithelial atrophy. In the presence of carcinoma of the breast, Beatson[9] advocated bilateral oophorectomy as a procedure of treatment. He believed the carcinoma progression was thus stopped when ovarian influence was removed. Ahlbom[3] observed 163 patients with breast carcinoma who were castrated by roentgen irradiation. He came to the conclusion that roentgen castration was of little benefit except in a small group of menstruating women past forty-five years of age. Martin[103] stated that routine castration in young women with breast carcinoma was hardly justifiable. Taylor[145]

recommends the direct opposite—routine castration because of the likelihood of carcinoma occurring in the other breast with subsequent pregnancy.

Martin,[103] Dresser,[34] and others, have noted distinct improvement of metastatic bone lesions following roentgen castration in women before the menopause. These findings suggest a close association but adequate proof is wanting.

Careful clinical observations of patients receiving estrogens are being made by many medical groups but to date no authentic reports have been offered to indicate that breast carcinoma is produced by the estrogens.

Summary. Experimental evidence has demonstrated that estrogens are important in the development of carcinoma of the breast in certain strains of mice. These strains are limited to those in which carcinoma of the breast appears spontaneously. Many authors have worked in this field and practically all have reached this conclusion. In the rat, there is some evidence to indicate that estrogens will induce carcinoma of the breast. As yet this finding has been reported by only one or two authors. In all other experimental animals, including the monkey, estrogens have failed to induce carcinoma of the breast.

In the human female, there have been many reports suggesting the etiological importance of estrogens in the development of carcinoma of the breast. Conclusive demonstration of this contention is wanting. Numerous reports concerned with estrogenic therapy in the human female have been made. In no instance has carcinoma of the breast been unequivocally demonstrated to directly result from the administered estrogens.

CARCINOMA OF THE CERVIX

Experimental Evidence

Mouse: Loeb and his coworkers reported a precancerous lesion of the cervix in a mouse after prolonged estrogenic therapy (Loeb, Burns, Suntzeff, and Moskop[98]). This finding has been confirmed in a large series of mice and extended in that the lesion in one mouse was metastatic and transplantable (Gardner, Allen, Smith, and Strong[55]).

Rats, guinea pigs, and rabbits have been given prolonged treatment with estrogens as noted in the preceding section. No cervical carcinomas have been reported.

Monkey: In 1933 Overholser and Allen[121] reported "precancerous changes" in the cervix of a monkey given estrogenic treatment plus local trauma of the cervix. However, other workers were unable to confirm these findings. Hisaw and Lendrum,[72] Migliavacca,[111] Zuckerman[162] and the original reporters in a later paper classified the cervical changes produced as a hyperplasia (Overholser and Allen[122]).

Clinical Inference

It has been noted repeatedly that the cervical epithelium undergoes cyclic changes in association with the menstrual cycle (Wollner[158]). During pregnancy the epithelium is subjected to marked hormonal stimulation (Hofbauer[73]). It has been shown that carcinoma is more common in multiparous women (Cullen,[27] Mattmüller,[104] Hofmeier,[74] and others). Hofbauer[73] believes that the predilection of cervical carcinoma for multiparous women is due to this marked stimulation of the epithelium rather than to the cervical inflammation or trauma incident to delivery. The cervical epithelium, however, is much less stimulated and altered than the endometrium and the breast and yet carcinoma of the cervix is the most common malignant lesion in the female. Such would suggest that factors other than an endocrine one are essential for the development of carcinoma of the cervix. Another fact enhancing this latter contention is that Cullen[28] found endometrial hyperplasia in only 2.4 per cent of the patients with cervical carcinoma. It seems most probable that any estrogen present in adequate amount to stimulate the cervical epithelium with resulting carcinoma development should al-

so induce some demonstrable epithelial response in the much more readily stimulated endometrium. The marked epithelial changes observed in the monkey during pregnancy and following estrogenic therapy have not been found in the human. No carcinoma has been reported in the human cervix following the injection or use of the various estrogenic substances.

Summary. There is suggestive evidence that estrogens have produced carcinoma of the cervix in the mouse but in no other experimental animal. There is only meager evidence that the estrogens have any influence in the development of carcinoma of the cervix in the human female.

CARCINOMA OF THE ENDOMETRIUM

Experimental Evidence

In the *rat*, *mouse*, *guinea pig*, *rabbit*, and *monkey* estrogens have been given over prolonged periods of time. No carcinomatous changes have been reported. This should not be confused with the few reported endometrial carcinomas obtained by treating animals with estrogens plus chemical carcinogens (dibenzanthracene) (Perry,[125] Perry and Ginzton[126]).

Clinical Inferences

A relationship between carcinoma of the endometrium in the human female and estrogenic substances has been postulated. The fact that the endometrium is markedly stimulated and physiologically altered by the estrogens immediately suggests the potential power of these substances. The profound changes so produced have been variously classified as hyperplasia. It is generally accepted that hyperplasia results from unopposed estrogenic effects (Fluhmann,[45] Witherspoon,[154] Graves,[62] Novak and Martzloff,[119] Burch and Burch,[15] Meyer,[109] Schröder,[135] and others). Demonstration of direct transition from hyperplasia to adenocarcinoma would enhance the theory of an endocrine cause of endometrial carcinoma. Ewing[41] reported 3 cases of carcinoma arising in hypertrophied glands overlying submucous fibroids. Horsley[76] found an adenocarcinoma in a patient who four months previously had had a hypertrophied endometrium as demonstrated by a dilatation and curettage. Bamforth[8] observed an early carcinoma in a hyperplastic endometrium. Bäcker[7] reported a patient that was curetted twenty times in ten years for uterine bleeding. The first seventeen curettages revealed "endometrial glandularis." The eighteenth and nineteenth curettage specimens were diagnosed as adenoma benignum, and the twentieth time definite adenoma malignum was found. Taylor[146] reported 85 cases of endometrial hyperplasia, 2 of which later developed carcinoma. Mazzola[105] reported hyperplasia in an eighteen year old girl which was followed in eight months by development of an adenocarcinoma. Fluhmann[44] observed 6 cases of squamous cell metaplasia in glands of hyperplastic endometriums. Three of these were malignant and 3 were benign. Taylor,[146] and Novak and Yui[120] observed hyperplastic glands adjacent to a region of carcinoma which they believed was a significant finding.

On the other hand, Hintze[70] studied 24 cases of hyperplasia and found no carcinoma in any. Fluhmann and Stephenson[46] stated that there were few cases of carcinomatous changes in hyperplastic endometrium. Taylor[146] concluded that such reports suggested that the estrogenic substances were etiologically important, although this was not yet a conclusively proved fact.

A consideration of such data must include another fact. Carcinoma of the endometrium is almost always found in women after the menopause. Of 61 such patients studied at St. Luke's Hospital, 57 were beyond the menopause. Thus, any intimate association of hyperplasia and carcinoma would indicate that hyperplasia is principally a post-menopausal condition. On the contrary, hyperplasia of the endometrium occurs usually during the menstrual life. Although hyperplasia is reported in post-menopausal women by Taylor and

Millen,[147] other reports suggest that these changes are not true hyperplastic ones but are rather senile and regressive ones. Taylor remarked, in discussing a paper by Mazzola,[105] that the type of hyperplasia noted in the menopause or just before the menopause did not in all probability give rise to carcinoma. He suggested that the type of hyperplasia associated with carcinoma development varied from the classical hyperplasia.

Taylor[144] observed cystic ovaries in patients with endometrial carcinomas. He suggested that this might indicate the importance of an endocrine disturbance as an etiological factor. Herrell[68] also found cystic ovaries. He concluded "that the unopposed action of estrin with its resulting effect on the endometrium is the basic principle in the development of malignancy of the endometrium in those individuals who possess the genetic factor necessary for the development of cancer." The group of 61 patients studied at St. Luke's Hospital rarely revealed cystic ovarian changes (Brewer). That some endocrine factor is associated with endometrial carcinoma development was intimated by Crossen and Hobbs[26] who noted a late onset of the menopause in patients that later developed carcinoma. Additional evidence is suggested by the fact that approximately one-fifth of patients with endometrial carcinomas also have fibroids (Davis,[31] 21.3 per cent; Norris and Vogt,[118] 20.8 per cent). Herrell[68] stated that he had not seen an endometrial carcinoma in a castrated patient. It does not seem unusual that endometrial carcinoma is rarely seen in surgically castrated patients. As a rule, when the ovaries are removed a hysterectomy is also done. Accordingly, the number of such patients in whom endometrial carcinoma might develop is small. This fact plus the comparative infrequency of endometrial carcinomas in all types of patients in all probability explains the rare occurrence of an endometrial carcinoma in surgically castrated patients. In patients who have been castrated by roentgen or radium irradiation, endometrial carcinomas have been occasionally found. Corscaden in a discussion of a paper by Mazzola[105] reported the development of endometrial carcinomas in 3 instances in a series of 1,500 patients who had been previously castrated by irradiation.

Finally, this type of carcinoma has not been observed following the clinical use of estrogens.

Summary. There is no evidence that estrogens have produced carcinomas of the endometrium in experimental animals. Although numerous clinical reports suggest a close association between estrogenic stimulation of endometrial tissues and the development of carcinoma in these tissues, there is no definite evidence that such an association exists.

CARCINOMA OF THE VULVA

Animal experimental evidence is completely wanting in this lesion.

Clinical Inference

Carcinoma of the vulva in the human female occurs in almost all instances after the menopause. The association between this type of carcinoma and hormones is had chiefly in the fact that it frequently develops subsequent to leukoplakia and kraurosis of the vulva (Taussig,[141] Goldberger,[61] Brewer,[14] and others). Many authors consider that these latter conditions are directly associated with an endocrine disturbance (Taussig,[141] Meigs[107]). When they occur before the menopause, there is usually some menstrual disturbance (Goldberger[61]). They are strictly limited to the vulvar skin. The skin of the vulva is readily affected by the estrogens (Foss[49]). Foss described marked growth of the squamous epithelium of the vulva and hyperemia of the deeper tissues. He observed rapid healing of a vulvar ulcer and possible regression of kraurosis in a patient treated with large doses of estrogens. Estrogens may relieve the symptoms temporarily but their administration does not cure or alter the pathological course of events. Even though

estrogens may produce epithelial cell growth in the vulva, there are no reported instances of carcinoma developing as a sequel. The numerous other etiological causes given for these vulvar conditions suggest that the direct causal factor is still undetermined.

NONMALIGNANT TUMORS OF THE BREAST

Experimental Evidence

Mouse: Adenomas, glandular hyperplasias, and multiple cysts have been produced in the mouse by prolonged treatment with estrogens (Wiesner,[153] Gardner, Smith and Strong[57]).

Rat: Similar lesions have been produced in the rat (Herold and Effkemann,[64,66] McEuen, Selye, and Collip,[102] Astwood and Geschickter[6]).

Guinea pig: A lone report has appeared that "sebaceous metaplasia" may be produced in the breast of the guinea pig by prolonged estrogenic therapy (Florentin and Binder[43]).

Rabbit: Hyperplastic pathological changes have been produced in the rabbit with estrogens (McDonald[99]). These changes, however, are definitely self limited and regress in spite of continued administration of estrogens.

Monkey: Monkeys have been given long continued treatment with estrogens (in particular by Folley and Zukerman[48]). No reports have appeared that estrogens have caused nonmalignant tumors of the breast in this species.

Clinical Inference

Some authors have claimed that estrogens cause pathological changes in the breast (Lewis and Geschickter,[92] Cheatle[19]). Other workers have advocated treating the same pathological conditions with estrogens (Cotte, Pallot, and Bérard;[22] Cutler;[30] Rogers and Nathanson[130]). Taylor and Brown[148] reported relief of symptoms in patients following radiation of the ovaries.

Summary. In the mouse, rat, guinea pig, and rabbit, breast changes have been produced by estrogens. In the monkey and the human, relationship between the estrogens and such changes have not been conclusively demonstrated. This relationship seems plausible, however, from a clinical standpoint.

NONMALIGNANT TUMORS OF THE CERVIX

Experimental Evidence

Mouse and rat: Both of these species of animals have a non-glandular cervix. While carcinomas and precancerous lesions have been reported, no nonmalignant tumors due to treatment with estrogens have been reported.

Guinea pig: No tumor formation has been induced in the guinea pig with estrogens. However, a squamous metaplasia of the glandular epithelium has been noted (Nelson;[116] Dessau[32]).

Rabbit: Lacassagne[84] has reported an adenomatous proliferation of the cervix in this species after prolonged estrogen administration.

Monkey: Overholser and Allen[121,122] have produced what is probably a squamous metaplasia. This finding has been confirmed (Migliavacca;[111] Hisaw and Lendrum[72]). Zuckerman[162] has studied this lesion in detail and found that such cervices return to normal when the administration of estrogens is stopped.

Clinical Evidence

Squamous cell metaplasia, although not a true tumor formation, should be mentioned. It occurs frequently in the cervical epithelium and is thought by some to result from excessive estrogenic stimulation. Taylor[144] reported marked metaplasia in the cervical glands in a patient with a granulosa cell tumor. Hofbauer[73] observed unusual activity of the cervical squamous epithelium during pregnancy. Since estrogenic substances are abundant in such instances, it is believed that they exert the stimulating effect. It is an accepted fact that certain tissues, such as breast, uterus, vagina, cervix, etc., are stimulated by estrogenic hormones. That the squamous cell metaplasia noted in the human cervix

is a direct result of such stimulation is not a proved fact but it is strongly suggested.

The significance and importance of the squamous cell metaplasia is not completely understood. That these lesions are associated with or are the forerunners of carcinoma has been suggested but not proved. Schiller[133] and Hinselmann,[69] in fact, observed that precancerous areas are not located in these regions of maximum stimulated epithelium but rather are found in the regions of normal epithelium.

Summary. Epithelial changes in the cervix have been produced in experimental animals with estrogens. Some epithelial changes observed in the human female have been considered the direct result of estrogenic substances. These changes in both experimental animals and humans have not been demonstrated to be etiologically important in the development of carcinoma.

NONMALIGNANT TUMORS OF THE ENDOMETRIUM

Experimental Evidence

Pathological changes have been produced in the endometrium of a variety of animals. These changes, however, cannot be classified properly under the heading of tumors. In all probability these changes produced with estrogens in each case regress to normal when treatment is discontinued.

Mouse: Relatively short treatment with estrogens has produced cystic hyperplasia (Parkes;[123] Gardner, Allen, and Strong[53]). Prolonged periods of treatment have caused a squamous metaplasia of the normal cuboidal or columnar endometrial epithelium (Gardner, Allen, and Strong[53]).

Rat: Squamous metaplasia has been produced (McEuen;[100] Selye, Thomson, and Collip;[136] Kaufmann and Steinkamm;[79] Herold and Effkemann;[65,66] Zondek;[161] Korenchevsky[80]) and with shorter periods of treatment a cystic hyperplasia has been described (Wolfe, Campbell, and Burch;[158] Burch, Williams, and Cunningham[16]).

Guinea pig: Estrogens have been noted to cause a cystic hyperplasia in the guinea pig (Nelson;[116] Dessau[32]).

Rabbit: A cystic hyperplasia of the endometrium has been produced in the rabbit (Pierson;[127] Lacassagne;[84] Zondek[159]).

Monkey: Similar lesions have been produced in the monkey and chimpanzee (Zuckerman and Morse;[164] Zuckerman[163]).

Clinical Evidence

Hyperplasia, which is not a true tumor formation in the human, has been discussed briefly in association with carcinoma of the endometrium. Hyperplasia has been produced in castrated women by the injection of estrogens (Werner and Collier;[151,152] Kaufmann[78]). It has been found in association with granulosa and theca cell tumors (Taylor;[144] Geist and Gaines;[58] Melnick and Kanter[108]). Hintze[71] reported squamous cell metaplasia associated with estrogenic stimulation and Taylor[144] also stated this metaplasia might be present with hyperplasia. Fluhmann[44] observed such metaplasia in the glands of hyperplastic endometrium.

Summary. Both the experimental and clinical evidence indicates that endometrial changes such as hyperplasia and squamous cell metaplasia are the direct result of estrogenic stimulation. It is not definitely known, however, what relationship these changes have to the development of true tumors. It seems possible, as Taylor (see Mazzola[105]) noted, that some type of epithelial hypertrophy or hyperplasia precedes carcinoma development.

NONMALIGNANT TUMORS OF THE MYOMETRIUM

Experimental Evidence

Mouse: In spite of long continued treatment with estrogens in many laboratories no myometrial tumors have been reported in this species.

Rat: No myometrial tumors have been reported in this animal.

Guinea pig: Fibromyomas have been produced in this animal by long periods of treatment with estrogens. The production of this tumor by estrogens in the guinea

pig has been reported by several workers (Nelson;[116] Dessau;[32] Moricard and Cauchoix;[112,113] Lipschütz and Iglesias[93]).

Rabbit: Lacassagne[84] has reported the production of myometrial fibromas in rabbits after prolonged estrogen administration.

Monkey: No myometrial tumors have been produced in the monkey.

Clinical Inference

An intimate relationship between the development of uterine fibroids and ovarian dysfunction has been accepted clinically for many years. Evidence suggesting this is that fibroids invariably develop during the stage of active ovarian and menstrual life. Fibroids cease to grow after the normal or artificial menopause. Radiation castration to stop the growth and symptoms of fibroids is a clinical utilization of this fact. Meyer[110] in refuting the ovarian dysfunction theory believed that the dependence on the ovary was fundamentally one of blood supply. Supporting Meyer's contention, Dichtl[33] reported that fibroids associated with extensive vascular adhesions might continue to grow after the menopause in the presence of atrophic ovaries.

During pregnancy rapid growth of fibroids has been repeatedly observed. In numerous instances, however, the enlargement of the fibroids is not a true growth phenomenon, but is rather an increase in size as a result of increased vascularity, edema, and various degenerative changes. The contention that the increased estrogenic concentration during pregnancy produces a rapid growth of fibroids has been accepted but not definitely proved.

Uterine bleeding, a frequent symptom of fibroids, is thought to be the result of an associated ovarian disturbance in the majority of instances. Since uterine bleeding and uterine fibroids are so frequently associated, many authors consider this evidence of a common endocrine origin of both. Ovarian changes have been repeatedly observed in patients with fibroids (Albrecht;[4] Popow;[128] Witherspoon[154,155]). These changes, as reported, were principally failure of ovulation and the formation of multiple follicular cysts. Meyer[110] argued that fibroid development was not based directly upon ovarian causes since many of these patients menstruated and ovulated normally. Häggström[63] failed to find cystic ovarian changes in any unusual frequency.

A frequent association of hyperplasia of the endometrium with fibroids has been observed (Witherspoon[155]). Since hyperplasia is the result of estrogenic stimulation, it was concluded that fibroid formations were likewise a direct result of prolonged and unopposed action of the estrogens (Witherspoon[155]).

Sterility and dysmenorrhea in patients with fibroids (Freund;[50] Albrecht[4]) has suggested to many authors that an endocrine imbalance was closely associated with fibroid development. Meyer,[110] however, pointed out that many patients with fibroids do become pregnant. It seems probable that the frequent sterility in these patients is, as Curtis[29] suggested, "dependent upon an interference with the development and delivery of the fetus, rather than the prevention of conception."

The development of endometriosis and adenomyosis is considered to be dependent upon the action of estrogenic substances by some authors (Adler;[2] Meyer[110]). In support of this it has been noted that the lesions occur only during the menstrual life of a patient. The lesions atrophy after normal and artificial menopause (Graves[62]). In the absence of ovaries, atrophy can be prevented by the use of estrogen (Gleave[60]). These lesions are frequently in association with uterine fibroids (Smith;[138] Allen;[5] Witherspoon[156]). These and other workers consider the estrogens as a common etiological factor. The occurrence of endometrial hyperplasia and cystic ovarian changes in association with endometriosis has suggested the same conclusion. Since endometriosis is frequently associated with sterility, some authors stated this was additional evidence of the existence of an endocrine disturbance.

In some instances carcinoma has been reported to have developed in an endometriosis lesion (Sampson;[131] Reinhardt;[129] Höppner[75]). This does not indicate, however, that carcinoma is intimately associated with estrogenic stimulation but, as Taylor (see Mazzola[105]) noted, the possibility of an indirect association seems tenable.

Summary. Fibromyomas have been produced in the guinea pig and rabbit by administered estrogens. Similar lesions have not been produced in other experimental animals. In the human there is some evidence that estrogens are associated in some way with the development of fibromyomas and endometriosis. There is good evidence that the estrogens are essential for the growth of these lesions once they are established.

EXPERIMENTAL EVIDENCE AS TO THE EFFECT OF OTHER HORMONES ON TUMOR FORMATION

Carcinoma of the Breast in the Mouse

Reports have appeared that the administration of androgens prevents or inhibits the appearance of carcinoma of the breast in mice of a high spontaneous cancer strain (Flaks and Ber;[42] Nathanson and Andervont[115]). From the data presented, however, one cannot conclude that the administered androgens have directly inhibited the appearance of breast carcinoma. The administration of the androgens was started in young animals and continued for a long period of time. This type of treatment causes an inhibition of the anterior pituitary gonadotropic function with resulting ovarian atrophy or physiological castration. The lack of normal incidence of breast carcinoma in these mice is similar, then, to the result obtained when the animals are operatively castrated. Further support of this view is adduced by the fact that simultaneous administration of androgen with estrogen does not influence the incidence of breast carcinoma when compared with that obtained with estrogens alone (Lacassagne;[87] Gardner[52]). Progesterone also does not inhibit the breast carcinoma inducing effects of administered estrogens (Lacassagne;[87] Gardner[52]).

One report has appeared that the administration of thyreotropic hormone (thyroid stimulating hormone of the anterior pituitary) prevents the appearance or decreases the incidence of carcinoma of the breast in mice (Cramer and Horning[25]). However, a repetition of this work by Lacassagne[88] failed to confirm these findings.

Fibromyomas in the Guinea Pig

Lipschütz and Vargas[96] have claimed that fibromyomas are more readily produced in the castrated guinea pig with estrogens than in guinea pigs in which the ovaries are present. More recently Lipschütz, Murillo, and Vargas[94] have contended that the factor in the animal's ovary that furnishes this limited protection against the fibromyoma producing power of estrogens is progesterone. They have reported a small series of animals in which the guinea pigs receiving both progesterone and estrogen had fewer tumors than the group receiving estrogens alone. This finding, if confirmed by other workers, or in larger series of animals, may possibly be of some significance. At the present time clinical implications cannot be made.

Cervical and Uterine Metaplasia

As has been noted, long continued treatment with estrogens has caused metaplasia of the cervical epithelium in the monkey and of the uterine epithelium in the rat and mouse. These metaplasias may not be classified as true tumors but it is of interest to note that this metaplasia producing power of estrogens may be directly antagonized by simultaneously administered progesterone. This has been demonstrated for the cervix of the monkey by Zuckerman[162] and for the rat endometrium by Korenchevsky.[80]

EFFECT OF HORMONES ON GROWTH OF ESTABLISHED TUMORS

Pregnancy with its marked increase in hormone concentration increases the incidence of carcinomas of the breast in the mouse but it has been shown that pregnancy does not influence the growth of already established carcinomas (Loeb[97]). Emge and Murphy[38] have demonstrated that rapidly repeated pregnancies do not uniformly increase the rate of growth of mammary adenofibromas in rats, nor do repeated pregnancies alter the morphological character to a greater extent than a single pregnancy. Similarly, it has been shown that pregnancy does not influence the rate of growth of transplants of three different types of sarcomas in rats (Emge, Schilling, and Wulff[37]).

While Nitta[117] found that castration of the mouse host inhibited the growth of a transplanted carcinoma and sarcoma, his work is confusing in that he found that administered estrogens also inhibited the growth of these tumors. He listed the findings of fifteen authors who have done experimental work on the influence of estrogens on tumor growth in mice. Seven authors found that estrogens had no effect, seven found growth was inhibited and one found growth was accelerated. Two more recent reports have appeared to the effect that estrogens do not influence the rate of growth of established tumors (Zondek;[160] Gardner[52]).

From these rather confusing reports, one can fairly safely conclude that administered estrogens or states that increase the estrogen concentration (pregnancy) do not significantly increase the rate of growth of established tumors in the experimental animal. This is not in agreement with clinical impressions in the human.

In the application of data having to do with the effects of hormones or even dietetic considerations on the growth of tumors, one must remember that tumors must have nourishment and probably will not grow as rapidly in sick as in well animals. The long continued administration of high doses of estrogens has a deleterious effect on the health of the experimental animal. This factor may explain the few reports that estrogens inhibit the growth of established tumors.

Reports have appeared that irradiation (Bischoff, Maxwell, and Ullman[10]) or extirpation of the pituitary gland (Samuels and Ball[132]) inhibit the rate of growth of tumors. An animal with its pituitary damaged or removed is not a well animal. Its nutrition and metabolism are definitely at a low grade. It may be expected that tumors in such animals grow more slowly than in normal animals. There is no proof then that the pituitary has any direct or specific effect on the rate of tumor growth.

QUALITATIVE AND QUANTITATIVE CONSIDERATIONS

Sufficient experimental evidence has been cited to establish the fact that estrogens have a definite influence on the formation of true tumors in certain experimental animals. In this regard several very important and pertinent points can be easily overlooked.

Species Differences

Most of the physiological functions of estrogens are truly nonspecific and apply in general to all animals. This is not true of its tumor inducing effects. The incidence of carcinoma of the breast may be increased in the female mouse. Carcinoma of the breast may be induced in the male mouse of cancer susceptible strain. Cancer of the breast may be induced in certain strains of rats. But in no other species of experimental animals has such an effect been observed. Carcinoma of the cervix may be induced in the mouse, but in no other species has such an effect been produced. Fibromyomas may be induced in the guinea pig and possibly in the rabbit, but in no other species has such an effect been demonstrated.

Intra Species

In considering the tumor inducing po-

tentialities of estrogens, another important factor should be kept in mind. Cancer of the breast cannot be induced in all mice, nor apparently in all rats. In mice, it has been definitely demonstrated that another factor in addition to the estrogen must be present for carcinomas to occur. Carcinomas result only in estrogen treated male or female mice that come of a strain that spontaneously develops breast carcinomas. Carcinomas are not produced in mice of a strain that never have spontaneous breast carcinoma. An inherent tendency to breast carcinoma, then, is of fundamental importance and a necessary factor in the experimental animal for its production. Inasmuch as breast carcinomas have been produced with regularity in the rats of only one laboratory and not in other laboratories, the same factor seems to hold true for rats.

Quantitative Considerations

In the induction of breast carcinomas a direct quantitative dosage factor has been demonstrated in the mouse (Suntzeff, Burns, Moskop, and Loeb;[140] Gardner[51]) and the rat (Geschickter[59]). Within the limits of experimental error certain doses must be given to induce or increase the incidence of breast carcinoma in the mouse. Dosages below this level have no effect. Dosages above this level cause a greater percentage incidence of breast carcinomas in the experimental series.

The dosage which has increased the incidence of breast carcinoma in female mice, or caused it to appear in male mice of susceptible strains, has varied with different workers. Inasmuch as exactly what should be considered the physiological dose or minimal effective dose (mouse unit) varies widely in different laborato-

TABLE I

DIRECT EXPERIMENTAL EVIDENCE AS TO TUMOR FORMATION BY ESTROGENS

		Mouse	Rat	Rabbit	Guinea Pig	Monkey	Human
Malignancies	Breast	+	+	o	o	o	o
	Cervix	+	o	o	o	o	o
	Endometrium	o	o	o	o	o	o
	Vulva Vagina	o	o	o	o	o	o
	Ovary	o	o	o	o	o	o
Nonmalignancies	Breast	+	+	±	±	o	o
	Cervix*	o	o	+	+	+	o
	Endometrium*	+	+	+	+	+	+
	Myometrium	o	o	+	+	o	?
	Vulva Vagina	o	o	o	o	o	o
	Ovary	o	?	o	o	o	o

* Changes produced may or may not be classified as "tumors."

ries, only approximate estimates can be considered in regard to the dosage factor. However, a review of the various reports shows that a dosage equivalent to 50 to 500 times physiological amounts are administered to mice to obtain breast carcinomas. In Geschickter's[59] work on the rat the lowest average dosage that caused carcinoma of the breast was at least 50 times the physiological dose for this animal.

A similar dosage factor has been demonstrated in the production of fibromyomas in guinea pigs (Lipschütz, Rodriguez, and Vargas[95]). Thirty times the physiological dose was the minimal amount that produced these tumors.

Another factor that must be considered in relation to estrogens and tumor formation is the necessary length of time during which treatment must be given to produce such lesions. In the mouse, treatment must be extended over a period representing one-tenth or one-half of the total life span of the animal to induce carcinoma of the breast. In the rat, the necessary time has varied from one-sixth to almost two-thirds of the total life span of the animal to produce a similar lesion. In the guinea pig, treatment must be given during one-tenth to one-half the life span of the animal to produce fibromyomas. The same factors hold true in regard to other nonmalignant changes that have been produced in various animals. Dosages of estrogens many times the physiological amounts must be given for prolonged periods of time to produce such effects.

There has been a widespread tendency on the part of both clinicians and laboratory workers to transfer results obtained in animal experiments directly or by inference to the human. While no doubt the vast majority of such assumptions turn out to be true, the essential validity of such a method is doubtful. The possibility of species differences in response to procedures or administered drugs must always be considered.

Species differences in regard to the tumor inducing power of estrogens have been demonstrated to exist. But dismissing this valid objection, and presupposing that all the different tumorigenic actions of estrogens demonstrated in various animals automatically apply to the human, it is of interest to calculate the necessary dosages for the human. On a weight for weight basis, and with the dosage used by many workers to induce carcinoma of the breast in the mouse (0.05 mg. estradiol benzoate per week), a human female would have to be given about 120.0 mg. per week or 17.1 mg. (171,000 I.B.U., or about 100,000 R.U.) per day of estradiol benzoate to produce a similar lesion. Transferring the minimal dosage used to produce carcinoma of the breast in the rat, the human female would have to be given 12.5 mg. (125,000 I.U.) of estrone daily.

It is of interest to note that the monkey, a species much closer to man than the mouse or rat, has been given an average dosage of a little more than 0.5 mg. of estrone daily (equivalent on a weight basis of 5.0 to 7.5 mg. to the human) for periods as long as 484 days with no resulting malignant breast changes.

A further important consideration in presuming to transfer results obtained in the rat or mouse or guinea pig to the human would be the necessary length of the period of treatment. There is some experimental evidence in the work with true chemical carcinogens (tar, dibenzanthracenes, methylcholanthrene, etc.). The necessary length of the period of treatment to produce malignancies in various animals varies directly with the total life span of the animal (Passey[124]). If it is valid to consider this matter in relation to total life span, the human female would have to be treated continuously for a period of ten to thirty years to obtain carcinoma of the breast as it is produced in the rat or mouse.

CONCLUSIONS

It is quite possible that the authors have inadvertently omitted pertinent findings in this review. However, on the basis of a survey of the available literature, we be-

lieve that several general remarks are justifiable.

The cause of certain tumors in certain animals has been definitely established. The administration of certain dosages of estrogens for certain periods of time have caused specific tumors in the mouse, rat, guinea pig, and rabbit. Filterable viruses cause specific tumors in the fowl and in the rabbit. Certain chemical carcinogens cause specific tumors in the mouse, rat, rabbit, and dog.

On the other hand, experimental evidence is difficult to obtain in the human. While certain tumors in the human may be due to specific chemical carcinogens (bladder tumors in dye workers), the general cause of tumors in the human is not known. Genetic factors, irritation, chemical carcinogens, filterable viruses, sex hormones, and even other etiological factors have all had their proponents. The various "proofs" of the importance of each of these factors have of necessity been by inference only.

The authors of this review do not believe that there is sufficient evidence to clearly establish that any one factor, such as estrogens, is the sole important etiological agent in the production of malignant or nonmalignant tumors in the human female. There is insufficient evidence available to lead to the assumption that estrogens, as produced in the body or as administered by the physician, have directly caused tumor formation in the human.

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DISCUSSION

DR. H. O. JONES, Chicago. The subject of the relation of the sex hormones to tumor formations of the female reproductive system encompasses a wide field, and the literature on this subject is voluminous. The authors have been able to cover only a limited portion of this field due to time limitations. A few additional topics of general interest should be mentioned.

It is generally accepted clinically that castration decreases and pregnancy increases the growth of established breast carinomas. From this assumption the inference is drawn that castration inhibits the tumor growth because it removes, or at least markedly decreases, the concentration of estrogens in the body. Conversely it is thought that pregnancy increases the rate of tumor growth since it increases the concentration of estrogens.

We know that results obtained from animal experimentation cannot and should not be directly applied to the human, but it is of interest to note that the results obtained from animal experimentations disagree with these assumptions.

Although various workers have shown that pregnancies do increase the incidence of breast carcinoma in the mouse, Loeb has shown that pregnancies do not influence the growth of already established carcinomas. Nitta found that estrogens inhibited the growth of transplanted carcinomas in the mouse. He listed fifteen authors who had done experimental work in this field. Seven men found that estrogens had no effect, seven found that estrogens inhibited the growth of the tumors, and only one man found that estrogens accelerated the growth. More recently, Gardner and Zondek found that estrogens did not influence the growth of established tumors in the mouse.

In the rat, Emge and his coworkers have found that pregnancy did not influence the rate of growth of three different types of transplanted malignant tumors. They found that pregnancies had no uniform effect on the rate of growth of mammary fibroadenomas.

The effect of other sex hormones on tumor formation are considered. This is only of academic interest at the present time, but Flaks and others have claimed that the continuous administration of male sex hormone (testosterone) inhibits or partially prevents the appearance of breast carcinomas in mice of a strain that normally have a high spontaneous incidence of this lesion. They inferred that the male hormone had a direct anti-tumorigenic action. It is well known that when mice of this susceptible strain are castrated in infancy they do not develop breast carcinomas, as the authors indicated in one slide. Estrogens from the ovaries are one of the factors necessary for its development in these animals. By the continuous administration of the male hormone they caused physiological atrophy of the pituitary gland. The atrophied pituitary gland no longer stimulated the ovaries. Consequently the ovaries atrophied and a true physiological castration ensued. The results obtained by these authors then was identical with that which is obtained by operative castration.

This view is supported by the work of Gardner, and we have found that mice receiving both the male hormone and estrogens had as many breast carcinomas as mice receiving just estrogens. It is apparent then that male sex

hormone does not have a direct anti-tumorigenic action in the experimental animal. Experiments by Gardner also have shown the same thing is true with progesterone, the hormone of the corpus luteum. These substances, however, nullify the ability of estrogens to produce certain lesions in the female genital tract that are not true tumors.

Zuckerman and others independently demonstrated that progesterone and probably testosterone if given in sufficient doses will correct the supposedly estrogen-induced uterine hyperplasia in the human.

In closing, it might be well to stress the point made by the authors of the distinct species specificity of the tumorigenic action of estrogens and to deplore hasty assumptions that the results which have been obtained in only one or two species of animals necessarily will be the same in the human female.

In addition it is worth stressing again the tremendously large and totally unphysiological doses of estrogens that must be given to animals to obtain tumors. These are doses that even the most improvident of physicians will never approach in magnitude.

PHARMACOLOGY OF HUMAN BLOOD AFTER ITS EXPOSURE TO ROENTGEN RAYS*

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MY INTEREST in the effect of ultraviolet and roentgen rays and radium emanations on the blood of higher animals dates back to 1924, when I discovered that living plant-physiological test objects are much more sensitive indicators than living zoöpharmacological test objects of minute quantities of toxic substances in blood and by their use demonstrated in certain sera the presence of various toxins not detectible by ordinary methods. By this means I demonstrated the presence of "menotoxin" in blood of women at time of catamenia.[1] By the phytopharmacological method also a specific toxin was found in the blood of patients with pernicious anemia, a toxin not demonstrable in sera of other types of anemia.[2] Employing the same methods, Macht and Hill exposed human sera in vitro or in quartz tubes to ultraviolet and roentgen rays and to radium emanations. Subsequent phytopharmacological examination of these bloods, irradiated outside the body, i.e., in quartz tubes, revealed that while ultraviolet rays did not affect their toxicity, treatment with roentgen rays and radium made them more toxic than they were normally. These findings were taken into account when I commenced the present study of blood sera obtained from a series of individuals before and also after their exposure to roentgen rays.[3]

In a preceding issue of this JOURNAL I[4] have described the results derived from special phytopharmacological examination of blood samples taken from normal animals before and after their exposure to roentgen rays. Such specimens were obtained from mice, rats, guinea pigs, kittens, dogs and other animals in normal health. They were then given varying doses of roentgen rays, after which a second sample was secured from each animal, usually on the following day. The samples of normal and irradiated blood sera were respectively examined by the phytopharmacological method and it was found that from twenty-four to forty-eight hours after exposure the blood of normal animals exhibited a marked toxicity lasting for several days and then gradually disappearing. Such a finding indicated that some toxic substance was developed in the blood twenty-four or forty-eight hours after exposure to the roentgen rays.

In the present paper I am reporting the findings which I obtained in such studies on human subjects, some in normal health and others suffering from various diseases. Blood sera were secured before and then after their treatment with roentgen rays. Phytopharmacological tests were made with 1 per cent solutions of the sera in Shive solution.[5] Most of the subjects examined were patients in the roentgenologic clinic of the Johns Hopkins Hospital, but specimens were obtained also from clinical cases in various other Baltimore institutions. Some of these cases were receiving roentgen therapy for benign affections such as hypertrophy of tonsils and myoma, while others were being irradiated for malignant disease (cancer). A few cubic centimeters of blood serum were obtained from each case shortly after admittance to the roentgenologic clinic and then again twenty-four to forty-eight hours after roentgen irradiation.

RESULTS OBTAINED

The blood sera of 30 patients, male and female, have now been studied by the phytopharmacological method after roentgenological treatment. Results obtained in the first sixteen cases studied in this manner

* Read at a meeting of the Optical Society of America, New York, February 23, 1940.

are shown in Table I. Some of these patients, it will be noted, suffered from malignant disease, chiefly cancer metastases, while others did not, but the findings obtained in the two sets of cases were similar. A marked increase in toxicity of the blood, as indicated by lowered phytotoxic indices, was noted in all the cases studied. This toxicity usually proved greatest twenty-four to forty-eight hours after exposure to roentgen rays and gradually decreased thereafter, becoming normal in seven or eight days. Generally the toxicity varied in intensity with the dosage of roentgen rays administered but the number of cases studied so far is too few to warrant specific correlation between dosage and the pharmacological findings.

TABLE I

EFFECT OF ROENTGEN RAYS ON BLOOD OF CLINICAL CASES

Case No.	Diagnosis	Phytotoxic Index		Time Elapsing between Roentgen Treatment and Taking of Specimen	Dosage Employed
		Before Treatment	After Treatment		
		per cent	per cent		
N 17	Carcinoma of breast	73	45		200 r
N 17	Carcinoma of ovary	74			No x-rays
M.B.M.	Hypertrophied tonsils	72	37	24 hours	
		72	72	8 days	
105391	Carcinoma of breast	68	42	48 hours	265 r
180902	Carcinoma of cervix	52	45	48 hours	156 r
181248	Carcinoma of breast		77	48 hours	160 r
174802	Carcinoma of prostate	79	46	24 hours	260 r
175925	Syringomyelia	73	56	24 hours	101 r
159409	Myoma	61	41	24 hours	270 r
174976	Carcinoma of submaxillary gland	66	58	24 hours	198 r
169275	Eustachian salpingitis	69	30	24 hours	129 r
176084	Hypertrophic nasopharyngitis	72	41	24 hours	160 r
183874	Carcinoma of breast	84	40	24 hours	202 r
170813	Carcinoma of breast	66	58	48 hours	194 r
181423	Chancre of tongue	69	64	24 hours	2×160 r
Mrs. Y	Carcinoma of breast	68	32	24 hours	300 r

EXAMINATION OF NORMAL SUBJECTS

These striking toxicological findings suggested an inquiry as to whether exposure to roentgen rays of personnel engaged in roentgenological work and enjoying apparently good health effects any change in their blood that is detectible by the phytopharmacological test. Through the courteous cooperation of various physicians I secured samples of blood from a number of roentgenologists, technicians and other assistants employed in roentgen departments of several Baltimore hospitals. Table II shows the phytotoxic indices of blood specimens from 28 such individuals: 5 were physicians, 19 were roentgen technicians or nurses, 1 was an orderly, and 2 were stenographers or clerks. It will be noted that all but three of the sera gave toxic readings. The phytotoxic index of normal human blood is 75 per cent. A normal reading was given by the blood of one of the subjects, a technician engaged in a roentgenologic clinic for but a very short period. On the other hand, the serum of Mrs. B. (No. 19), a technician employed in such a department for several years, gave also a practically

TABLE II

BLOOD PHARMACOLOGY OF RADIOLOGISTS AND THEIR STAFFS

No.	Subject	Occupation	Phytotoxic Index	No.	Subject	Occupation	Phytotoxic Index
			per cent				per cent
1	Average control (normal blood)		75	15	Tol.	Technician	52
2	J. H. 30	Technician (for a few weeks)	64	16	Clapp	Technician (for four months)	50
3	J. H. 31	Technician	57	17	Mohr	Technician (for six years)	42
4	J. H. 33	Technician	55	18	Kohl	Technician	42
5	J. H. 34	Technician	51	19	Mrs. B.	Technician	68
6	J. H. 36	Technician (for very short period)	75	20	Mr. Hall	Technician (for five years)	60
7	J. H. 38	Technician	43	21	Pridgeon (colored)	Orderly	62
8	J. H. 39	Technician	33	22	Broad	Stenographer	83
9	J. H. 40	Technician	59	23	Abbau	Stenographer (for four years)	58
10	Fishb.	Technician (for twelve years)	41	24	Dr. A.	Physician-Radiologist	50
11	Cohen	Technician (for eight years)	36	25	Dr. D.	Radiologist	42
12	Snyder	Technician (for three years)	39	26	Dr. K.	Radiologist	42
13	Hol.	Technician	47	27	Dr. M.	Radiologist (new)	60
14	Kelly	Technician	56	28	Dr. W.	Radiologist (for twenty years)	47

normal figure, a reading only serving to emphasize the phytotoxicity of sera of the other subjects. Again, specimen No. 22 had an index slightly higher than that of normal blood. I am not prepared to explain this reading although it has been demonstrated that a very high phytotoxic index may also indicate an abnormal condition, e.g., a virus disease.[6]

COMMENT

The results of this preliminary study, made on the sera secured from a series of individuals before and also after their exposure to roentgen rays, show clearly that such therapy effects a pathological change in the blood. The change was even more strikingly demonstrated in apparently healthy physicians and their staffs, whose

TABLE III

BLOOD PHARMACOLOGY IN RELATION TO ROENTGEN EXPOSURE
(Each of Six Solutions Tested on 25 Seedlings)

Solution of Serum from	Increment of Root Growth	Phytotoxic Index	Standard Deviation (σ) =	Probable Error (P.E.) =	Critical Ratios
	mm.	per cent			
(Shive control)	10.8	100	1.48	0.199	
Normal human	7.2	68	1.60	0.135	Shive control to normal serum = 15
Roentgen-ray patient	5.3	49	1.64	0.220	Normal serum to roentgen-ray serum = 8
Radiologist	4.8	45	1.36	0.183	Normal serum to radiologist's serum = 11
Roentgen-ray technician	4.8	45	1.16	0.156	Normal serum to roentgen-ray serum technician = 12
Roentgen-ray clerk	5.4	51	1.095	0.148	Normal serum to roentgen-ray clerk serum = 9

sera gave low phytotoxic indices. In Table III a comparison is made of the readings given by normal human blood and sera secured respectively from a patient receiving roentgen therapy, a roentgenologist, a technician and a clerk in a roentgenologic clinic. Statistical analysis of each phytopharmacological experiment and calculation of the standard deviation and probable error yielded critical ratios definitely establishing the validity of the experimental readings.

I propose to study a larger series of cases in this way and also to determine by phytopharmacological means whether the various forms of medication advocated for roentgen sickness have any detoxifying effect.

SUMMARY

1. Blood specimens obtained from a series of patients both before and after their exposure to roentgen rays and examined phytopharmacologically revealed a marked toxicity twenty-four to forty-eight hours after such treatment.

2. Such toxicity was exhibited not only by sera from cases of cancer but also by blood specimens of patients suffering from non-malignant pathological conditions and cannot therefore be ascribed to resolution of tumors and absorption of their products of decomposition for I have shown that phytotoxic readings have been given by sera of normal animals after their exposure to roentgen rays.

3. Blood specimens from a number of roentgenologists and technicians engaged in roentgenologic clinics for considerable periods of time also gave low phytotoxic indices despite the apparently good health of the respective individuals.

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Twenty-sixth Annual Meeting: Hotel Cleveland, Cleveland, Ohio, June 2–3, 1941.

EDITORIALS

JOINT MANIFESTATIONS ASSOCIATED WITH INTRATHORACIC TUMORS

THE enormous literature which has accumulated within the last few years dealing with primary cancer of the lungs has stimulated the roentgenologist in his efforts to arrive at a diagnosis of a suspected lesion of the lung at an earlier stage than has hitherto been done, and one recalls with a great deal of vividness the axiom of Manges that roentgenologists must become "carcinoma of the lung minded" if they are to make a diagnosis of carcinoma of the lung when it might be amenable to therapy. Following this injunction and the stimulating remarks of others, there is no doubt that carcinoma of the lung is being diagnosed at an earlier stage and much more frequently than it was even a few years ago.

Recently Van Hazel,* in a very thought-provoking article, has called attention to the joint manifestations associated with intrathoracic tumors. He notes a striking fact that joint manifestations may constitute the initial complaint in intrathoracic tumors. It has long been known that clubbing of the fingers occurs in such diseases as bronchiectasis, chronic lung abscess, or heart disease, but Van Hazel says that less common are the joint manifestations of hypertrophic pulmonary osteoarthropathy which, when occurring rapidly as a primary complaint, can easily be mistaken for arthritis. Its chief symptoms are clubbing of the fingers, with swelling, pain, tenderness, and in some cases, an accompanying elevation of temperature probably due to the primary disease.

Van Hazel reports seven cases in which the initial symptom was joint changes. In five cases malignancy of the lung was proved, and in two a benign tumor was present. The striking manifestation in these seven cases was that there was a complete absence of symptoms referable to the chest from one month to one year after the onset of joint symptoms. One of his cases, namely a case of bronchiogenic carcinoma upon whom a pneumonectomy was performed, was followed by an immediate disappearance of all arthritic symptoms in spite of the fact that this patient had been bedridden and helpless for six months because of painful joints.

The onset of the joint involvement in the cases which he reports was either a stiffness or swelling accompanied by some pain. In three of the seven cases the symptoms had an abrupt onset and in four a gradual onset. In all of the cases he reports there was clubbing of the fingers, but this manifestation was overshadowed by the swelling, pain, and disability of the joints. Curiously enough, six of his patients were treated for arthritis. The arthritic process was of such a disabling nature that four of his seven patients were confined to bed but in none of these cases were the chest symptoms annoying except during hemoptysis in one patient with bronchiogenic carcinoma. The fingers and hands were enlarged giving the appearance of swelling without a pitting edema, and a dusky cyanosis was present. The skin of the hands was usually moist; flexion of the fingers caused varying degrees of pain. The bones showed the typical periosteal proliferation particularly of the ulna, radius, tibia, and fibula, and, in some, of the metacarpal and metatarsal bones. Curiously enough some of the patients had remissions in their symptoms for a time; there was slight temperature elevation.

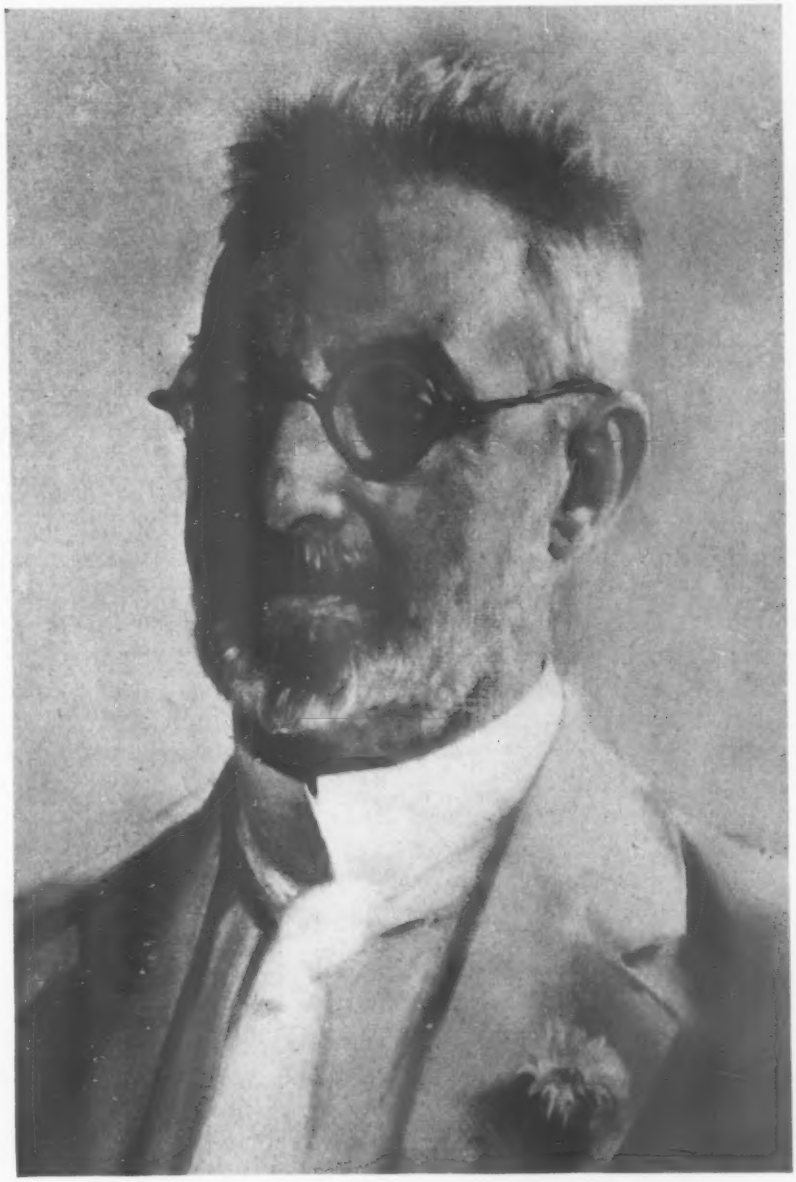
* Van Hazel, Willard. Joint manifestations associated with intrathoracic tumors. *J. Thoracic Surg.*, 1940, 9, 495–505.

The occurrence of hypertrophic pulmonary osteoarthropathy has been known since the reports of Bamberger and Marie in 1890. Locke, in a very extensive study on pulmonary osteoarthropathy, reported 144 cases including five cases of his own. In this group the respiratory tract was the site of the primary disease in 108, and also in this group tumors of the mediastinum, pleura or lung occurred in nine patients. Locke was able to study some of his cases over a long period of time and from his roentgenographic studies he concluded that the subperiosteal proliferation loosely attached to the shaft of the bone in the early stages might later become fused, compact bone, that the proliferation in the advanced cases might become generalized and later in the disease the bone changes might include erosion of cartilage, lipping about the joint and, in some instances, ankylosis, and that exacerbations of the primary disease caused simultaneous increased swelling, pain and tenderness in the joints and increased activity in the bone, while remissions occurred when the primary lesion subsided.

Many attempts have been made unsuccessfully to create this condition in experimental work, notably by Bamberger, Phemister, Compere and Adams, Churchill, and others. Campbell, in his experimental work, had the unusual opportunity to secure a finger during life which showed marked clubbing. In his study of this specimen he found the enlargement was due to edema which separated the connective tissue fibers, and the greatest thickening occurred between the bone and the nail bed. He was unable to demonstrate increased fat or fibrous tissue thickening, and there was an absence of pitting. But he cites Widal's observation as an explanation of this, namely, that the tissues are capable of taking up considerable amounts of water before the clinical sign of pitting manifests itself. Van Hazel calls attention to the further support of this theory in the prompt disappearance of swelling, cyanosis, pain and disability in his cases following the removal of the tumor. Campbell believes that the decrease in oxygen tension brought about by the faulty aeration of the blood which passes through the lung is one of the factors bringing about the changes seen in the hands and feet, and that this anoxemia, which varies in degree, leads to edema where the circulation is slow, namely in the extremities. Campbell observed that in the various conditions reported producing osteoarthropathy there is no obstruction to the venous return but a varying amount of lung tissue has ceased to fulfill its proper function.

It is known that only a relatively small percentage of intrathoracic tumors are associated with osteoarthropathy and those that do show osteoarthropathy are the ones in which chronic anoxemia exists, and the location of the tumor in relation to the blood vessels, particularly the pulmonary veins, plays an important part in the production of the malady.

Van Hazel, in the report of his cases, has called attention to a very important observation, namely that hypertrophic pulmonary osteoarthropathy may be the initial symptom in intrathoracic tumor and that the condition may simulate an arthritic process, the complete absence of chest symptoms masking the etiological factor. He lends further support to the belief that faulty aeration of the blood in the involved lung may bring about a chronic anoxemia as a causative factor of osteoarthropathy.



CHRISTIAN DEETJEN
1863–1940

IN THE cause of truth and in the advancement of human knowledge, no sacrifice has been more spectacular than the slow torture which so many of the pioneers in roentgenology were called upon to endure. Tribute is paid to these martyrs not only in monuments of stone, but also in the gratitude in the hearts of all radiologists who succeeded them. More than two hundred of these pioneer investigators paid with limb and life that radiologic science should advance. The names of the more famous are forever on the lips of radiologists, but there are many others whose heroism is unsung, who suffered just as gallantly, who made valuable scientific contri-

butions, and who are virtually unknown to members of the profession today. Such a person was Dr. Christian Deetjen, of Baltimore, who finally paid with his life on December 28, 1940, after nearly forty years of suffering.

Georg Adolph Christian Deetjen was born August 29, 1863, in Buenos Aires, Argentina. He was graduated from the University of Würzburg, Germany, in 1890. While a student there, he attended lectures in physics given by Professor Röntgen. He came to the United States and settled in Baltimore, where he became associated with the late Dr. H. Chandlee, and began to work with roentgen rays in 1900. In March, 1901, he established himself as one of the first specialists in roentgenology in Baltimore, in an office at 21 West Franklin Street. Until his retirement in 1930, he did roentgenologic work for many private physicians and hospitals, and was connected with the Maryland Medical College, the Maryland General Hospital, and the Howard A. Kelly Sanatorium.

During his early active years, he kept in close contact with other roentgenologists, both in this country and in Europe. He was a member of the American Roentgen Ray Society in its early years, and he was made a diplomate of the American Board of Radiology. He visited European medical centers (Levi-Dorn, Albers-Schönberg, Immelmann, Walther, Haenisch) for study in 1902, 1904, 1907, and 1910. On the first of these trips, he saw Röntgen in Munich. He probably was the first in Baltimore to make roentgenograms of kidney stones and of brain tumors. In 1902 he treated skin diseases with roentgen rays, especially many cases of psoriasis. Later, he began the treatment of carcinoma, and obtained good results in epithelioma, some success in carcinoma of the breast, and in sarcoma, but no success in malignant lesions of the stomach. No patient of his ever was burned by the roentgen rays.

The first symptoms of his own injury from the rays appeared in 1902, when he suffered from the characteristic dermatitis, first on the left hand and later on the right. The first extensive skin grafting operation was performed on his left hand by Dr. Porter, in Boston. Later, he had repeated operations in Baltimore, with the loss of several fingers. In 1929, the left hand had to be amputated, and he had many keratoses and excruciating pains in the right hand.

Dr. Deetjen's devoted wife, Alma, preceded him in death by only four days, and the ashes of both rest in a single urn in Druid Ridge Cemetery, in Baltimore.

To those who knew him, Dr. Deetjen's serenity combined with a fine sense of humor, and his courage through all his suffering, was a source of great inspiration.

In commenting on his death, the Baltimore *Sun* paid a fine tribute to his spirit, as follows: "Dr. Deetjen, being no fool, lamented without reserve the ignorance that trapped him; but he knew that snares and pitfalls lie in wait for any man who tries to extend the boundaries of knowledge, and that those who escape them owe their immunity largely to good fortune. If he had had it to do over again, there is no doubt that he would have chosen again the path of the investigator; for while he regretted his ignorance in the early days, he never regretted having tried to push back a little the edge of the great darkness that surrounds us all. Not even years of pain made him regret it; not even in the Valley of the Shadow of Death did he regret it. . . . A spirit so unperturbed, so blithe in the very presence of the Arch Fear was also a contribution to mankind; and those fortunate enough to feel its influence may be excused if they look upon the spirit of the man as a greater thing than any sort of intellectual triumph in the field of scientific research."

Otto Glasser

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. C. B. Peirce, Royal Victoria Hospital, Montreal, Canada. Annual Meeting: Cincinnati, Ohio, Sept. 23–26, 1941.

American College of Radiology
Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago, Ill. Annual meeting: Hotel Statler, Cleveland, June 4, 1941.

Section on Radiology, American Medical Association
Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: Cleveland, Ohio, June 2-6, 1941.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting, 1941: To be announced.

Radiological Section, Baltimore Medical Society
Secretary, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May.

Radiological Section, Connecticut Medical Society
Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets bi-monthly on second Thursday, at place selected by Secretary. Annual meeting in May.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. H. W. Ackemann, 321 W. State St., Rockford, Ill.

Radiological Section, Los Angeles Co. Med. Soc.
Secretary, Dr. Wilbur Bailey, 2007 Wilshire Blvd., Los Angeles, Calif. Meets on second Wednesday of each month at County Society Building.

Radiological Section, Southern Medical Association
Secretary, Dr. Roy G. Giles, Temple, Texas.

Brooklyn Roentgen Ray Society
Secretary, Dr. L. J. Taormina, 1093 Gates Ave., Brooklyn, N. Y. Meets monthly on fourth Tuesday, October to April.

Buffalo Radiological Society
Secretary-Treasurer, Dr. Joseph S. Gian-Francheschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months, place of meeting selected by the host.

Chicago Roentgen Society
Secretary, Dr. C. J. Challenger, 3117 Logan Blvd. Meets second Thursday of each month October to April inclusive at the Palmer House.

Cincinnati Radiological Society
Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to May, inclusive.

Cleveland Radiological Society
Secretary, Dr. H. A. Mahrer, 10515 Carnegie Ave. Meets at 6:30 P.M. at Mid-Day Club rooms on fourth Monday each month, October to April, inclusive.

Denver Radiological Club
Secretary, Dr. P. R. Weeks, 520 Republic Bldg., Denver, Colo. Meets third Friday of each month.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

Florida State Radiological Society
Secretary, Dr. J. N. Moore, 210 Professional Bldg., Ocala, Florida. Meetings in May and November.

Georgia Radiological Society
Secretary, Dr. R. C. Pendergrass, Prather Clinic Bldg., Americus, Ga. Meets in November and at annual meeting of Medical Association of Georgia in the spring.

Illinois Radiological Society
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meetings held quarterly, on the fourth Sunday of the month.

Indiana Roentgen Society
Secretary, Dr. C. C. Taylor, 23 E. Ohio St., Indianapolis, Ind. Meeting held the second Sunday in May annually.

Kentucky Radiological Society
Secretary, Dr. J. C. Bell, 402 Heyburn Bldg., Louisville. Meets annually in Louisville on third Sunday afternoon in April.

Long Island Radiological Society
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:30 P.M.

Michigan Association of Roentgenologists
Secretary, Dr. J. E. Lofstrom, 1536 David Whitney Bldg., Detroit. Three meetings a year, Fall, Winter, Spring.

Milwaukee Roentgen Ray Society
Secretary, Dr. I. I. Cowan, Mt. Sinai Hospital, Milwaukee, Wis. Meets monthly on first Friday at University Club.

Minnesota Radiological Society
Secretary, Dr. J. P. Medelman, 572 Lowry Medical Arts Bldg., St. Paul.

Nebraska Radiological Society
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

New England Roentgen Ray Society
Secretary, Dr. A. O. Hampton, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

Radiological Society of New Jersey
Secretary, Dr. W. J. Marquis, 198 Clinton Ave., Newark. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

New York Roentgen Society
Secretary, Dr. E. J. Ryan, St. Luke's Hospital, New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

North Carolina Roentgen Ray Society
Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

Central New York Roentgen Ray Society
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year. January, May, November.

Ohio Radiological Society
Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati. Meets at time and place of annual meeting of Ohio State Medical Association.

Pacific Roentgen Society
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport Pa. Meets annually.

Philadelphia Roentgen Ray Society
Secretary, Dr. B. R. Young, Temple University Hospital. Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

Pittsburgh Roentgen Society
Secretary, Dr. H. W. Jacox, 4800 Friendship Ave. Meets second Wednesday each month, 4:30 P.M., October to June, Pittsburgh Academy of Medicine.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. S. C. Davidson, 277 Alexander St. Meets on second Thursday from October to May, inclusive, 8 P.M., Rochester Academy of Medicine Building.

St. Louis Society of Radiologists
Secretary, Dr. W. K. Mueller, University Club Bldg. Meets fourth Wednesday of October, January, March and May, at a place designated by the president.

San Francisco Radiological Society
Secretary, Dr. H. A. Hill, 450 Sutter St., San Francisco. Meets monthly on third Thursday at 7:45 P.M., first six months at Toland Hall, second at Lane Hall.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

South Carolina X-Ray Society
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

Tennessee Radiological Society
Secretary, Dr. F. B. Bogart, 311 Medical Arts Bldg., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. L. W. Baird, Scott and White Hospital, Temple, Texas.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00–5:00 P.M., Room 301, Service Memorial Institute.

Virginia Radiological Society
Secretary, Dr. C. H. Peterson, 603 Medical Arts Bldg., Roanoke, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. K. J. Holtz, American Bank Bldg., Seattle. Meets fourth Monday of each month at the College Club, Seattle.

Cuba

Sociedad Cubana de Radiologica y Fisioterapia
Secretary, Dr. Francisco Padron, Enrique, Villuendas 64, Havana, Cuba. Meets monthly in Havana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets monthly on third Thursday from November to June inclusive, at 8:15 P.M., 32 Welbeck St., London.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine, 1, Wimpole St., London, W. 1.

Faculty of Radiologists
Secretary, Dr. M. H. Jupe, 32 Welbeck St., London, W. 1, England.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to November inclusive for scientific discussion.

Canadian Association of Radiologists
Secretary, Dr. A. C. Singleton, Medical Arts Bldg., Toronto, 5, Ontario.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext., Halifax, N. S.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

Continental Europe

Belgian Society of Roentgenology
Secretary, Dr. J. Boine, Avenue des Alliés, 134, Louvain (Belgium). Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Société de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel. Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale
Meets monthly on fourth Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, 11.52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aertze.
Permanent Secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Süd- und Westdeutsche Röntgengesellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Röntgengesellschaft
Meets annually in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the spring, and one in the fall.

Societa Italiana Radiologia Medica
Secretary, M. Ponzio, University of Turin, Prof. Turin.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Măräcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly on first Monday at 8 o'clock.

Polish Society of Radiology
Secretary, Dr. Jan Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. B. Krynski, 11 Zielna St. Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime.

Society of Medical Radiology in Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. G. Biering, Copenhagen. Meets the second Wednesday of each month from October to July in Copenhagen, at 8'oclock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Roentgen Society
Meets first Wednesday of each month, at 6:30 P.M. at Zentral-Röntgen Institut des allgemeinen Krankenhauses Alserstrasse 4.

Orient

Japan X-Ray Association
c/o Orthopedic Surgery, Tokyo Imperial University. Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto Japan. Meets bi-monthly on third Sunday.

BULLETIN OF THE INTER-SOCIETY COMMITTEE FOR RADIOLOGY

DOCTORS AND POLITICS

Time was, in the good old days, when the physician was looked up to by the citizens of his community as a sort of font of worldly wisdom. His advice and counsel were sought by his admiring neighbors in matter of health, domestic relations, and politics. As a fatherly imparter of practical wisdom, the old family doctor sometimes almost usurped the functions of the priest.

Admitting that the complexity of modern urban civilization has largely erased the intimate relationship which formerly existed between the doctor and his "families," it is nevertheless our premise that the physician can and should exert a more effective influence on political events than he does today. Before enlarging upon this premise, it is perhaps well that we define some terms.

The word "politics," we insist, should be shorn of that malodorous connotation which has attached to it as a result of the dubious practices of some of the more notorious big-city machines. Politics, or political science, is concerned with the conscious definite purpose of society to establish authority and to determine its functions. By "playing politics," our illustrious forefathers conceived our form of government; they established its authority and determined its functions. The doctor, like every other good citizen, has inherited a responsibility to exercise the rights and privileges by which the individuals of the state control its public policy. His educational advantages increase his responsibility in this regard and render his neglect of duty more reprehensible than less fortunate followers in the civic community.

It is in this enlightened meaning of the word that our political system is envied from abroad. It is this kind of responsible citizenship that prompted no less a cynic than G. B. Shaw to remark several years ago that, "You in America should trust to that volcanic political instinct which I have divined in you."

Now, the chief political interest of doctors as citizens today concerns the so-called "socialization" of medicine. Here is another term needing definition. It has been so bandied about since the days of Marx and Lasalle as to become completely bereft of meaning. The Socialist party disowns the word. It means one thing in Petrograd and another in Peoria.

Socialism is a philosophy, and to "socialize" is to accomplish, in one way or another, that philosophy. The aim of the socialist is to replace competition by cooperation, and profit seeking by "social service," whatever that may mean. A sober consideration of the socialist philosophy reveals two conspicuous facts: it requires a considerable degree of dictatorial authority in the state, and our own government has traveled a considerable distance toward its realization.

Returning now to the interests of medical men; just what did our President mean when he said, on October 31, 1940, "Neither the American people nor their government intend to socialize medical practice any more than they plan to socialize industry"? These were reassuring words to doctors. But, due to the unfortunate fact that the term "socialize" has an extremely fuzzy meaning, it is doubtful if anyone besides the President knows exactly what he meant by that statement.

Certainly he meant that the right to seek profit in the practice of their profession would not be denied doctors. But, did he mean that he was opposed to compulsory health insurance? Probably not.

In his message on the state of the union, delivered to Congress on January 6, the President declared that this was "no time to stop thinking about the social and economic problems," and, in itemizing the subjects which, in his opinion, the Congress should immediately take under consideration, he referred specifically to the "widening of opportunities for adequate medical care." Next day, Senator Robert F. Wagner, New York, announced that a comprehensive proposal for an expanded national health program in line with the President's

recommendation was being prepared for introduction in Congress. Senator Wagner, it will be recalled, was author of the National Health Act, proposed to the 76th Congress for the implementation of the recommendations of the President's National Health Conference committee. He also sponsored the National Hospital Construction Act. Neither of the bills reached a vote.

According to newspaper accounts, the Senator's new bill will combine both the previous ones. Included in the $90,000,000 appropriation for the first year, the bill will, according to reports, provide for $35,000,000 in contributions to states toward the operation of "approved plans for general medical care." It also would provide $9,000,000 for construction of Federally owned hospitals. The U. S. Public Health Service and Federal Security Agency are reported to be working on a plan to offer federally financed health care to workers in defense industries.

Enactment of these legislative proposals may not amount to the "socialization" of medicine. They would, nevertheless, provide for a considerable degree of political control over a large portion of medical practice in America. That is the very thing to which the medical profession has objected in opposing "socialized" medicine or government controlled health insurance. It is not compulsory health insurance per se that is objected to—it is the political control of medical practice which must perforce accompany a federally controlled system.

Whether or not "socialized" medicine and compulsory health insurance are one and the same thing is a question we need not now debate. The point is that medicine has always and will continue to object to any proposal that will place the delivery of medical care under the control of politicians. Doctors know that such a system would be contrary to the best interests of the public and that any advantages claimed for it would be more than compensated for by a host of palpable evils.

Which returns us to our original premise: that physicians should exert a more effective influence on political events than they do today. To protect the public welfare against politics in health, and to guard the profession of medicine against influences bound to retard its progress, doctors must take a more active interest in politics. No group outside the medical profession is competent to guide the policies of the government in matters of health. It is the responsibility of the medical profession to provide this guidance. Under our system of government there is one way, and only one way, that such responsibility can be exercised—and that is through political effort.

Two points must be understood if the political effort of individual doctors and medical organizations is going to have any effect upon the policies of the government. To fully appreciate them, it is going to be necessary that some firmly settled illusions be discarded. First, local politics is very much more important than national politics. Second, the primary is vastly more important than the general election. Any citizen can exert a great deal more influence upon the political trends of the national government by quietly interesting himself in the politics of his own neighborhood precinct than he can by writing brilliant letters to his congressman. Furthermore, he will find that the time to convince a politician regarding any fundamental issue is before the election, and not afterwards.

These are stirring times in America—times during which the cloak of "national defense" can be used to usher in radical innovations in the function of the national government. Now is the time for all good doctors to come to the aid of their nation. They can aid their nation and protect the interests of the people by once more occupying a prominent place in the civic and political life of their community.

AMERICAN BOARD OF RADIOLOGY

The following is a list of those who have been certified or granted additional certification during 1940:

1. Abraham, Adolph, New York, N. Y., Radiology
2. Addington, Ercell A., Spokane, Wash., Radiology
3. Africano, Scipio H., Union City, N. J., Diagnostic Roentgenology
4. Andersen, L. Milford, Brooklyn, N. Y., Roentgenology
5. Armao, Joseph, Philadelphia, Pa., Radiology
6. Armbruster, John L., Milwaukee, Wis., Radiology
7. Aulls, Ernst C., Washington, D. C., Roentgenology
8. Avery, Roscoe E., Barre, Vt., Diagnostic Roentgenology
9. Barrett, Henry A., New York, N. Y., Radiology
10. Beckstrand, Grant H., Long Beach, Calif., Therapeutic Radiology
11. Berman, Theodore M., Miami Beach, Fla., Diagnostic Roentgenology
12. Bettelheim, Frederick, New York, N. Y., Radiology
13. Bird-Acosta, Ignacio, Ithaca, N. Y., Roentgenology
14. Borow, Louis, Bound Brook, N. J., Radiology
15. Bowing, Irwin E., Kenosha, Wis., Roentgenology
16. Boyer, Helene N., Racine, Wis., Radiology
17. Brannon, Donald D., Cleveland, Ohio, Roentgenology
18. Brown, James M., San Francisco, Calif., Radiology
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20. Bull, Robert G., White Plains, N. Y., Roentgenology
21. Burton, William Y., Portland, Ore., Radiology
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23. Cashion, William R., Jamaica, L. I., N. Y., Radiology
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26. Cooper, Jesse R., Newcastle, Pa., Radiology
27. Crawford, J. Ramser, Flushing, L. I., N. Y., Diagnostic Roentgenology
28. Danielius, Gerhard, Chicago, Ill., Roentgenology
29. Davenport, Carroll S., Lansing, Mich., Radiology
30. deLalla, Emanuel, Utica, N. Y., Roentgenology
31. Delano, Percy Joseph, Chicago, Ill., Radiology
32. Dirks, Maitland S., Iowa City, Ia., Radiology
33. Dodds, Wemple, Crawfordsville, Ind., Radiology
34. Eberhard, Theodore P., Columbia, Mo., Therapeutic Radiology
35. Edson, George N., Jackson Heights, L. I., N. Y., Diagnostic Roentgenology
36. Ehrenpreis, Bernard, Brooklyn, N. Y., Radiology
37. Elsey, Edward C., Cincinncati, Ohio, Radiology
38. Emery, Clyde K., Pasadena, Calif., Therapeutic Radiology
39. Farrow, Joseph H., New York, N. Y., Therapeutic Radiology
40. Feaster, Annete M. B., St. Petersburg, Fla., Therapeutic Radiology
41. Felson, Benjamin, Indianapolis, Ind., Radiology
42. Ferrucci, Joseph, Framingham, Mass., Diagnostic Roentgenology
43. Fuchlow, J. Richard, Rapid City, S. D., Roentgenology
44. Galligan, Charles A. Jr., Monterey, Calif., Diagnostic Roentgenology
45. Galluccio, Anthony C., Bronx, N. Y., Diagnostic Roentgenology
46. Garcia, Manuel, New Orleans, La., Therapeutic Radiology
47. Gemmill, James R., Monnessen, Pa., Diagnostic Roentgenology
48. Gibbon, William H., Sioux City, Ia., Radiology
49. Gilmer, William P., Clifton Forge, Va., Roentgenology
50. Glaser, Leland F., Springfield, Mo., Radiology
51. Goldberg, Benjamin, Chicago, Ill., Diagnostic Roentgenology
52. Goldblum, Jacob, Uniontown, Pa., Radiology
53. Golding, Harry N., Paterson, N. J., Diagnostic Roentgenology
54. Governale, Vincent J., Long Beach, N. Y., Diagnostic Roentgenology
55. Graves, A. Judson, Jacksonville, Fla., Radiology
56. Gray, Edwin F., Terre Haute, Ind., Radiology
57. Greene, Theodore C., Shantung, China, Diagnostic Roentgenology
58. Grossman, Abraham, Chicago, Ill., Therapeutic Radiology
59. Guillium, William H., Asbury Park, N. J., Roentgenology
60. Hames, Frederick W., Pine Bluff, Ark., Therapeutic Radiology
61. Hamilton, Charles C., Claremont, N. H., Roentgenology
62. Harrington, Leo A., Brooklyn, N. Y., Radiology
63. Hartzell, Homer V. Jr., Seattle, Wash., Radiology
64. Hayden, Edward M., Tuscon, Ariz., Diagnostic Roentgenology
65. Hayes, Arthur W., Greenfield, Mass., Roentgenology
66. Held, Louis A., Brooklyn, N. Y., Diagnostic Roentgenology
67. Helper, Norton, Ann Arbor, Mich., Radiology
68. Herendeen, Ralph E., New York, N. Y., Radiology
69. Hinkel, Charles L., New York, N. Y., Radiology
70. Holding, Arthur F., Albany, N. Y., Radiology
71. Hrdlicka, George R., Brooklyn, N. Y., Roentgenology
72. Hulst, Henry, Grand Rapids, Mich., Radiology
73. Huston, Harold C., Eau Claire, Wis., Radiology
74. Huyler, Washington C., New York, N. Y., Diagnostic Roentgenology
75. Jaffe, Henry L., Chicago, Ill., Therapeutic Radiology
76. Jamison, Horace W., Los Angeles, Calif., Radiology
77. Jares, John James Jr., Sarasota, Fla., Radiology
78. Johns, Miles W., Utica, N. Y., Diagnostic Roentgenology
79. Johnson, Samuel H., Miami, Fla., Roentgenology
80. Johnston, Albert C., Berlin, N. H., Roentgenology
81. Johnston, George C., Orlando, Fla., Radiology
82. Kahlstrom, Samuel C., Bath, N. Y., Diagnostic Roentgenology
83. Keddy, Russell A., Stamford, Conn., Radiology
84. Kegerreis, Roy, Elmhurst, Ill., Radiology
85. Kimble, J. Norman, Takoma Park, Washington, D. C., Diagnostic Roentgenology
86. Kok, Harry, Benton Harbor, Mich., Radiology
87. Krause, George R., Cleveland, Ohio, Roentgenology
88. Kresch, Philip, Bayonne, N. J., Diagnostic Roentgenology
89. Landsman, Isadore J., New York, N. Y., Diagnostic Roentgenology
90. Lawrason, Douglas M., Albuquerque, N. M., Radiology
91. Ledbetter, Llewellyn N., Beaumont, Tex., Diagnostic Roentgenology
92. LeMone, David V., Columbia, Mo., Diagnostic Roentgenology
93. Levin, Ralph T., New York, N. Y., Radiology
94. Lieff, Abraham, New York, N. Y., Therapeutic Radiology
95. Liljencrantz, Eric, San Francisco, Calif., Therapeutic Radiology
96. Lowman, Robert M., Philadelphia, Pa., Radiology
97. Marting, Esther C., Cincinnati, Ohio, Therapeutic Radiology
98. Meachen, John W., Boston, Mass., Roentgenology
99. Mendelson, Emanuel, Brooklyn, N. Y., Radiology
100. Merrill, Walter H., Glenn Dale, Md., Radiology
101. Merrit, William H., New York, N. Y., Radiology
102. Meyers, Paul T., New York, N. Y., Radiology
103. Miller, Albert, Rochester, Minn., Radiology
104. Miller, Earl R., New Haven, Conn., Radiology
105. Miller, John Francis, Johnson City, N. Y., Radiology
106. Miller, Lawson E., New York, N. Y., Roentgenology
107. Miller, Wallace C., Boston, Mass., Radiology
108. Minton, Russell F., Ardmore, Pa., Diagnostic Roentgenology
109. Morrison, Harvey R., Boston, Mass., Radiology
110. Mucci, Lawrence A., New Britain, Conn., Radiology
111. Mufson, Samuel, New York, N. Y., Diagnostic Roentgenology
112. Nessa, Curtis B., Minneapolis, Minn., Radiology
113. O'Hara, Fred Summa, Springfield, Ill., Radiology
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115. Perillo, Januarius A., Olean, N. Y., Roentgenology
116. Petersen, Arthur S. J., Chicago, Ill., Roentgenology
117. Pinkston, Beth Tollan, Los Angeles, Calif., Radiology
118. Pinner, William E., Philadelphia, Pa., Radiology
119. Popoff, George D., New York, N. Y., Roentgenology
120. Potosky, Henry, New York, N. Y., Therapeutic Radiology
121. Root, Joseph C., Cleveland, Ohio, Roentgenology

122. Rosenblate, Adolph J., Chicago, Ill., Roentgenology
123. Rossitto, Anthony F., Wichita, Kan., Radiology
124. Roswit, Bernard, New York, N. Y., Therapeutic Radiology
125. Sagel, Jacob, Gary, Ind., Roentgenology
126. Schlein, William, Brooklyn, N. Y., Roentgenology
127. Schulz, Milford D., Boston, Mass., Roentgenology
128. Scott, Lawrence D., Nashville, Tenn., Radiology
129. Seedorf, Everett E., LaCrosse, Wis., Radiology
130. Shapiro, Abraham V., New York, N. Y., Radiology
131. Sharp, George S., Pasadena, Calif., Therapeutic Radiology
132. Sheedy, Leo P., Pittsburgh, Pa., Radiology
133. Sinberg, Samuel E., New York, N. Y., Roentgenology
134. Smith, Jesse W., Bishop, Honolulu, Hawaii, Radiology
135. Springer, Floyd A., Des Moines, Ia., Therapeutic Radiology
136. Squire, Everett W., Charleston, W. Va., Radiology
137. Staderman, Albert H., Philadelphia, Pa., Roentgenology
138. Stein, George H., Elizabeth, N. J., Diagnostic Roentgenology
139. Stein, Joseph, Hawthorne, N. Y., Radiology
140. Stewart, Calvin L., Abington, Pa., Radiology
141. Strusinski, Nicholas D., Jackson Heights, L. I., N. Y., Diagnostic Roentgenology
142. Sullivan, Joseph V., Flushing, L. I., N. Y., Radiology
143. Thorner, Rosalind, Philadelphia, Pa., Radiology
144. Truog, Clarence P., Miami, Fla., Radiology
145. Tschetter, David J., Canton, Ohio, Radiology
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147. Vance, Lewis A., Boston, Mass., Diagnostic Roentgenology
148. Vanlandingham, Homer W., Rockford, Ill., Radiology
149. Wang, Shao-hsun, Peiping, China, Radiology
150. Ward, Leo J., Elizabeth, N. J., Radiology
151. Waskew, William L., Chicago, Ill., Roentgenology
152. West, Warren B., Champaign, Ill., Radiology
153. Wickham, Jacob M., Iowa City, Ia., Radiology
154. Williams, James N., Fort Leavenworth, Kan., Radiology
155. Willis, Augusta E., Orangeburg., S. C., Radiology
156. Wissing, Egon G., Boston, Mass., Roentgenology
157. Wood, John P., Pearl Harbor, Hawaii, Roentgenology
158. Woutat, Philip H., Grand Forks, N. D., Radiology
159. Zaretzki, Louis E., Brooklyn, N. Y., Radiology
160. Zwerling, Henry B., Brooklyn, N. Y., Radiology

INSTITUTE OF RADIOLOGY

An "Institute of Radiology" was held on January 18, 1941, at Syracuse, New York, under the auspices of the Central New York Roentgen Ray Society, The Medical Society of the State of New York, Syracuse University, College of Medicine, and the Division of Cancer Control of the New York State Department of Health. The meeting was a highly successful innovation and venture, attended by over two hundred radiologists, surgeons, physicians and medical students. The arrangements were made by a committee of which Dr. Donald S. Childs was chairman. The Dean of the Medical College, Dr. Herman G. Weiskotten, presided. At an afternoon session the following addresses were given: "Physics for Radiologists," by Dr. Edith H. Quimby, New York City; "The Diagnosis and Treatment of Brain Tumors," by Dr. Merrill C. Sosman, Boston, Mass.; "The Indications and Limitations of Different Methods of Treating Malignant Tumors," by Dr. Ursus V. Portmann, Cleveland, Ohio; "The Radiosensitivity of Malignant Tumors," by Dr. Fred W. Stewart, New York City; and "The Cyclotron," by Dr. Stafford L. Warren, Rochester, New York. Others who discussed Cancer Control in New York State included Dr. James M. Flynn, President of the State Medical Society; Dr. Edward S. Godfrey, State Health Commissioner; Dr. Louis C. Kress, Director of the Division of Cancer Control. In the evening a dinner was held at the Hotel Syracuse at which an address was given by Dr. R. R. Spencer, Assistant Chief of the National Cancer Institute of the United States Public Health Service.

DEPARTMENT OF TECHNIQUE

Department Editor: Robert B. Taft, M.D., B.S., M.A., 105 Rutledge Ave. Charleston, S. C.

SUCTION TYPE ROENTGEN THERAPY CONE

By CARL B. BRAESTRUP *and* WILLIAM BIERMAN, M.D.
NEW YORK, NEW YORK

IN THE treatment of small superficial lesions it is generally desirable to limit the radiation to the pathological area. This may be accomplished by roentgen opaque shielding or by means of cones. However, there is always the possibility that the shielding shifts or the patient moves when cones are used. To obviate these difficulties we designed a cone whereby suction is used to hold it firmly over the area to be treated. In the case of the Chaoul or "contact" technique the problem becomes of particular importance due to the short target-skin distance and resulting high dosage rate,[1] about 10,000 r/min.

The suction cone described here was designed primarily for the "contact" or Chaoul type of roentgen tube, but the same cone may, with slight modifications, be used on other types of therapy equipment. The construction is shown in Figure

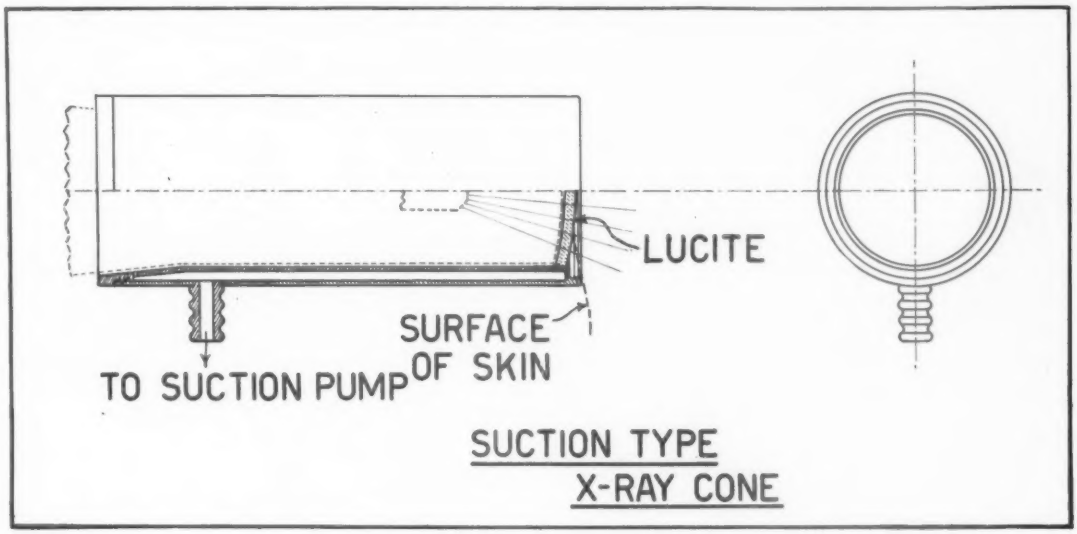

Fig. 1

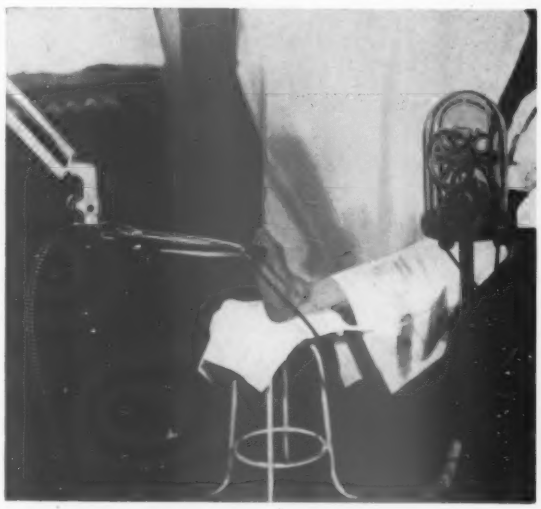

Fig. 2

[1] Braestrup, C. B., and Blatz, I. H. Physical factors of low voltage "contact" roentgen therapy. *Radiology*, 1940, *35*, 198–205.

1. The device consists essentially of two concentric brass tubings, the outer one of which is provided with a nipple for attachment of a hose to a suction pump. The inner tubing has a cap of "lucite" or of other transparent material of low roentgen-ray absorption (filtration equivalent to approximately 0.1 mm. Al). The cone is provided with various sized diaphragms which permit the use of fields up to 3 cm. in diameter.

The suction cone is placed over the lesion by observation through the "lucite" window. When the exact location has been obtained the suction pump is turned on and the pressure is reduced in the space between the tubings, thereby pulling the skin of the patient toward the window and holding it there. The "contact" or Chaoul roentgen tube is then inserted into the suction cone, or if the ordinary roentgen tube is used the tube holder is attached to the cone.

In Figure 2 is shown the use of the suction cone in the treatment of a wart on the foot at the Tumor Clinic and Radiation Therapy Department of the Morrisania Hospital where the cone has now been in use for several months. It is being used there to advantage in the treatment of most non-ulcerated lesions.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

HEAD

Maresh, Marion M. Paranasal sinuses from birth to late adolescence. 1. Size of the paranasal sinuses as observed in routine postero-anterior roentgenograms. *Am. J. Dis. Child.*, July, 1940, *60*, 55–78.

This report deals with the increase in size of the sinuses as evidenced in the routine postero-anterior roentgenograms and with the variations in the size of sinuses at different age levels. Tracings were made from the routine roentgenograms of the sinuses of 100 children who are being followed from birth to maturity at the Child Research Council. The youngest child was followed up to five years of age. The oldest child was followed up to seventeen years of age. Examinations were continual, beginning during the first month of life in most cases. The growth of the sinuses in these children is discussed in the paper and is illustrated by tracings and composite drawings.

Many variations of size and shape of antrums, ethmoid cells and frontal sinuses were observed. In almost every case, growth was a fairly uniform process as it concerned the antrums and ethmoid cells. The antrums sometimes appeared asymmetric in shape and size but the difference was not usually marked. The ethmoid sinuses appeared symmetric in almost every case.

The frontal sinuses on the two sides did not always begin to develop at the same time. Nor did one side consistently begin to develop before the other. The speed of their growth process was very irregular as compared with that of the antrums. In many instances a cell would begin to bud upward and after reaching a point definitely above the nasion would fail to increase in size in succeeding roentgenograms for some time. Later the cell might increase in size rapidly and either equal the size of the other frontal sinus or even become larger in a comparatively short time. There was no significant sex difference in time of appearance of the budding frontal sinus. The average age at which either frontal sinus was definitely above the level of the nasion and at which it began to increase in size was calculated as three years, although this is a difficult evaluation to make and might be interpreted differently by other examiners. The beginning frontal sinus was clearly seen in some children between one and two years of age, and in a few instances there was no evidence of a frontal sinus developing before six to eight years of age.

By superimposing the tracings made from roentgenograms of each child with the centers of each antrum on the same horizontal plane, the growth of the sinuses can be strikingly illustrated. Such studies of the growth of the antrums in individual children appear to illustrate better than measurements the futility of trying to establish a single "norm" representing either the size or shape of the sinuses at any given age. Tracings were arranged in order from the smallest to the largest antrums in each age group. It was noted that each child maintained a fairly constant position in the total group when the yearly tracings were arranged in order of size. That is, the children with the smallest antrums in one age group would also have the smallest antrum in the following age groups.—*R. S. Bromer.*

Dorrance, T. O. Lacuna skull (Lückenschädel). *Am. J. Dis. Child.*, Aug., 1940, *60*, 359–362.

Dorrance reports a case of lacuna skull in a boy who has reached the age of seventeen years. The majority of patients afflicted with this condition succumb during early infancy to either hydrocephalus or intercurrent infection. The patient has no accompanying meningocele or encephalocele. The roentgenograms of the skull showed lacunas and a large bony defect over the occiput.

The cause of lacuna skull is unknown but is believed to be (1) a primary disturbance in the development of the membranous bones of the calvarium, produced by ischemia, as well as (2) an increase in intrauterine intracranial pressure leading to pressure atrophy (nutritional and pressure atrophy).—*R. S. Bromer.*

Anzilotti, A. Reperto di "cranio a spazzola" in caso di malattia di Cooley infantile. ("Brush skull" in a case of infantile Cooley's disease.) *Radiol. med.*, May, 1940, *27*, 411–412.

In *Radiol. med.*, 1939, p. 720, Nicotra describes the bone changes in the skull and in the other bones in Cooley's disease (Mediterranean anemia). In this article the author reproduces the roentgenogram of "brush skull" seen in a case of this disease in a child five years of age. The case was one of typical Cooley's disease with mongoloid features, enlargement of the spleen, characteristic blood picture, etc. The case is particularly interesting because these changes are much more frequently seen in adults than in young children. There were other characteristic changes in the long bones and those of the pelvis and spinal column, but only the roentgenogram of the skull is reproduced, because of its rarity in childhood.—*Audrey G. Morgan.*

Foster, L. Paul. Cooley's syndrome (erythroblastic anemia) in a Chinese child. *Am. J. Dis. Child.*, April, 1940, *59*, 828–834.

Foster reports a case of Cooley's syndrome in a Chinese child of six and one-half years. This is the first case of erythroblastic anemia in a Chinese of which he can find any report. It is likewise one of the few cases reported in which the patient was not of one of the Mediterranean races. The mother of the patient has moderate anemia of the same type as the child and a suggestive roentgen picture. Foster considers this interesting, since erythroblastic anemia has been considered hereditary. It is possible that the mother may have a low grade erythroblastic anemia. The patient did not have as constant or as high a leukocytosis as has been generally reported. This is not, however, inconsistent with a diagnosis of Cooley's anemia. The roentgen examination showed the typical changes in the skull and long bones.—*R. S. Bromer.*

Agati, Dino. Selle turciche di frenopatici. (The sella turcica in mental defectives.) *Arch. di radiol.*, Jan.–Feb., 1940, *16*, 5–23.

The author made roentgen and anatomical examinations of 225 skulls from the Museum of the Psychiatric Hospital in Alexandria. The history was unknown in 29 of these cases but in 196 there was a history of mental disease or defect. Of these 66 were epileptics, 20 idiots, 34 moral delinquents and 76 suffered from the usual mental diseases. In only one of the 29 patients presumably normal mentally was there a monolateral fusion of the middle clinoid process with the anterior. But in 51 of the 196 cases of mental defect there were clinoid fusions, unilateral or bilateral, partial or total. Such fusions existed in 38 per cent of the cases of common mental disease, in 25 per cent of the idiots, 20 per cent of the criminals and 15 per cent of the epileptics.

The author discusses the various theories advanced to account for the causation of such anomalies of the sella and considers their relationship to certain forms of mental disease and endocrine disturbance. Some authors hold that they have no relation to mental disease but are caused by chronic inflammation of the region or are atavistic in origin as such pictures are seen normally in some of the lower animals. Gegenbauer and di Raggi say that such fusions are constant in the apes and consider that there may be an additional irritant factor in their development in man. Goldhamer and Schüller say that such fusions are not infrequently found in normal individuals. But the author examined 200 roentgenograms of normal individuals and found fusions in only 3.5 per cent, much lower than the percentage found in the dry skulls of patients with mental disease. He believes therefore that such malformations of the sella turcica play a part in producing mental disturbances and lesions of the mesencephalic nerve cells.

He also discusses the etiology of elongated dorsum. Goldhamer and Schüller think that it is a structure that exists in embryonic life. It is impossible to say definitely whether it is an anatomical variation or whether it has pathological significance. But the author describes a case in a girl of seventeen who at the age of seven had scarlatina followed by purulent otitis. As she grew older she suffered from mental torpor and attacks of prolonged sleeping. Roentgen examination showed an elongated dorsum sellae.

He presents some unusual malformations of the sella not detected by examination of the skull but shown in roentgenograms and also some detected anatomically not visible on roentgen examination, as for example a bridge of bone extending from one side of the tuberculum sellae to the quadrilateral lamina and enclosing the clinoid processes, 2 cases of elon-

gated dorsum and one case of segmented dorsum. He holds therefore that systematic roentgen examination of dry skulls may show some anomalies of the sella which have heretofore been thought by anatomists to be very rare and which have not been demonstrated by roentgen examination of the living skull because of the laws of roentgen projection and absorption of the rays.—*Audrey G. Morgan.*

AGATI, DINO, and BORTOLOTTI, RENATO. Protrusione endocranica di cellule etmoido-sfenoidali con sindrome oculo-chiasmatica. (Intracranial protrusion of ethmoido-sphenoidal cells with an occulo-chiasmatic syndrome.) *Arch. di radiol.*, Jan.–Feb., 1940, *16*, 24–31.

The authors present a peculiar case of abnormal intracranial development of ethmoid-sphenoid cells, manifested clinically by impaired vision.

The patient was a man of fifty-four; nothing of importance in the family or personal history. The present illness had begun about four years ago with progressive loss of vision, but up to January, 1938, the patient was able to work. During the month of April the disturbance of vision grew rapidly worse and he was obliged to give up his work. Examination by an oculist showed atrophy of the optic nerves and the patient was sent for roentgen examination. The patient had no other symptoms except the loss of vision. Examination of the urine and the Wassermann and Sachs-Georgi tests were negative.

Roentgen examination in the lateral projection showed an abnormal structure rising from the ethmoid-sphenoid plane. It projected for about 2 cm. upward into the cranial cavity, and its longest axis, the anteroposterior, was about 3 cm. long. It was semi-oval in shape and bounded above by an opaque line showing the consistency of bone. It was shown to be made up of various air-cells with thin septa between them. Some of these cells contained large posterior cells of the ethmoid labyrinth. The posterior boundary of the structure was a few millimeters from the tuberculum sellae. Both anterior and posterior clinoid processes showed signs of atrophy. The dorsum sellae showed an irregular structure probably due to atrophy. The sella was normal in size. In the oblique projections the optic canals were shown to be surrounded by large hypertransparent air-cells which protruded in front into the anterior fossa of the skull and posteriorly involved the clinoid processes. Apparently pressure from these cells had caused the atrophy of the optic nerves.

About six months later the patient had lost the sense of smell for some odors. There was evidently pressure on the frontal part of the chiasm.

If these air-cells had been a congenital anomaly the condition would have developed earlier in the patient's life. The growth of the sphenoid sinus and the ethmoid cavity generally stops between twenty and thirty years of age. The author concludes that there was some predisposing malformative element which had been acted upon later by some pathological factor. He does not know definitely what this was but is inclined to think it was not tumor formation but rather a reactive inflammation, probably from latent sinusitis. He has found no similar cases in the literature.—*Audrey G. Morgan.*

PENFIELD, WILDER, and KEITH, HADDOW M. Focal epileptogenic lesions of birth and infancy. *Am. J. Dis. Child.*, April, 1940, *59*, 718–738.

There is a group of epileptic patients whose history points to a cerebral lesion at the time of birth or during some febrile illness of infancy. The nature of these lesions which produce late habitual epilepsy has received scant attention up to the present. On the other hand, traumatic and ischemic cerebral injury has been studied exhaustively in autopsy series and relation of such injury to cerebral diplegia has been a subject of discussion for many years. The author's paper is based on a series of cases of habitual epilepsy in which the cerebral lesion dates back to birth or infancy, and a general report of the nature of these early lesions is given. All of the patients reported had craniotomy and radical excision of epileptogenic foci, but they were selected for this report only in order to throw light on the nature of these early lesions and on the fate of the brain which contains them, and not for an assessment of the value of surgical therapy. The lesions include focal microgyria, meningocerebral cicatrix and the cerebral cicatrix of arterial occlusion. They are apt to produce seizures. On the contrary, the authors have not been able to prove that old subdural hematoma of itself is a cause of epileptic seizures. It may often be associated with other lesions and

may be in a sense partly responsible for the associated intracerebral lesion which does produce epilepsy.

In considering the problem of initial cause in the case of any person with epilepsy, Penfield and Keith state that one must bear in mind the importance of minor cerebral lesions at birth and of thrombotic or inflammatory incidents in the febrile diseases of infancy, even though the onset of the seizures occurs only years afterward. In the study of such cases simple anteroposterior roentgenograms of the skull should be examined for proportional decrease in the size of one side of the skull. This may be taken as suggestive evidence of an early lesion of the type under consideration in their paper. Such lesions are often amenable to radical surgical therapy.

In one of their cases, pneumo-encephalogram, taken in the brow-up position, showed the septum pellucidum nearer the right than the left side. The right cranial chambers were much smaller than the left. There was also enlargement of the body of the right lateral ventricle. —*R. S. Bromer.*

Nielsen, Jens. Zwei Fälle von Ewing-Sarkom im Unterkiefer. (Two cases of Ewing's sarcoma in the lower jaw.) *Acta radiol.*, 1940, *21*, 286–291.

Two cases of Ewing's sarcoma at the angle of the lower jaw are described. Histological examination in both cases showed the typical picture of Ewing's sarcoma—a small round cell sarcoma with no differentiation of the cells.

The first case was in a man of fifty-one, first sent to hospital in May, 1931, for a swelling of the lower jaw. Roentgen examination showed destruction of bone at the angle of the jaw with spicules in the tumor. Operation was performed and the man remained free of recurrence for a year and a half. At the end of that time a recurrence developed in the scar. On January 18 and 24, 1933, he was given a dose of 60 per cent H.E.D. roentgen irradiation, through 0.5 mm. copper at a distance of 40 cm.; this dose was give over three fields—a relatively small dose but given in a short time. After five years the patient was free of any signs of local recurrence. But in November, 1937, prostatectomy was performed for enlargement of the prostate. Histological examination showed adenocarcinoma of the prostate.

The second case was in a boy of eighteen. In addition to the tumor at the angle of the right lower jaw he had an enlarged gland in the right maxillary region. Exploratory excision showed Ewing's sarcoma. Protracted fractional roentgen treatment was given from September 30 to December 17, 1934; total dose 7,000 r/l from three fields in the course of seven weeks—that is, an intense Coutard treatment. The tumor disappeared rapidly and five years later there were no clinical or roentgen signs of recurrence.

The results of irradiation alone in these tumors have been rather disappointing, so the rule has been quite generally adopted of operating first and giving prophylactic roentgen irradiation after operation. But tumors of this type are more or less biologically inoperable, even though technically operable. Therefore a careful record should be made of all cases like the second one above, that have been cured by irradiation alone. In this way it may be possible to prove that the treatment of choice of these tumors is protracted fractional roentgen irradiation with doses that do not cause any injury of bone.—*Audrey G. Morgan.*

NECK AND CHEST

Oliveri, Antonio. Tubercolosi infiltrativo-ulcerosa della laringe. (Infiltrative ulcerous tuberculosis of the larynx.) *Radiol. med.*, June, 1940, *27*, 490–492.

A man of thirty-five had a history of right exudative pleurisy at eighteen which had healed apparently without leaving any sequels. About a year ago he began to have a burning pain in the throat and his voice became weaker until he could hardly speak at all. Laryngoscopic examination showed marked infiltration of the right arytenoid and aryepiglottidean fold; it was very hard to see the glottis, but it was evident that the right vocal cord was greatly swollen and its posterior and middle thirds ulcerated. The left vocal cord seemed to be a little swollen.

Roentgenography of the larynx in the anteroposterior projection from above downward showed the hyoid bone normal; the left half of the epiglottis was normal, the right thickened at the aryepiglottidean fold. The vestibular part of the larynx was greatly deformed and decreased in size. A diagrammatic sketch and a roentgenogram of the findings are given. The left arytenoid was normal, the right greatly enlarged. The lumen of the glottis was deformed and stenotic. The right vocal cord was enlarged

and its free margin jagged; the left was slightly swollen. The rings of the cricoid and the base of the arytenoid cartilages were visible and partially calcified.

The chief roentgen finding in the right latero-lateral projection was a marked enlargement of the right arytenoid, giving it a proboscis-like appearance. The right aryepiglottidean fold was thickened, particularly in its middle third. The hyper-transparent image of the ventricle of Morgagni was ill-defined and stenotic.

The clinical and roentgen appearance in this case was that of tuberculosis of the larynx in the stage of infiltration and ulceration. Roentgen examination of the thorax showed bronchopneumonic foci scattered over the upper lung fields on both sides, most of them in the sclerotic stage, which tended to confirm the diagnosis made of the nature of the laryngeal lesions.—*Audrey G. Morgan.*

Huizinga, Eelco. Über die Enstehung der Bronchiektasie. (The origin of bronchiectasis.) *Acta radiol.*, 1940, *21*, 75–100.

The object of this article is to call attention to the fact that bronchography is of value not only in the diagnosis of bronchiectasis but also in studying the cause and course of this disease. Taking photographs in inspiration and expiration shows the influence of the respiratory movements. The peripheral bronchi show considerable variations of lumen on inspiration and expiration even under normal conditions and it is therefore easy to understand that bronchiectasis may develop even without contraction of the lung tissue when the bronchial wall is infiltrated and deteriorated. Cases of bronchiectasis following the swallowing of foreign bodies develop in lungs that have been absolutely healthy.

His bronchographic study of 100 cases leads the author to conclude that bronchiectasis is in the majority of cases an acquired disease. It often occurs at an early age following a pneumonia resulting from one of the acute infectious diseases of childhood, particularly whooping-cough or measles. Of course it is difficult to say that no congenital anomaly in the lung tissue existed before the pneumonia.

A case is described in a boy eight years of age in whom bronchiectasis developed after an acute infection. Large round dilatations persisted. It would be very easy on a later examination, if this history were not known, to diagnose a congenital bronchiectasis. Another point in demonstrating the infectious origin of the disease is the frequent coincidence of sinusitis and bronchiectasis. The author believes with Brauer that the mechanical causes of dilatation of the bronchi are a weakening and flabbiness of the wall of the bronchus caused by inflammation combined with external traction, from respiratory movements, for example, or from retraction. Atelectasis also is a factor in the causation of bronchiectasis. An acute bronchiectasis caused by a foreign body may heal entirely.

Among the author's 100 cases there were 39 following pneumonia, 8 in which pneumonia developed after the beginning of the symptoms, 33 following a long period of coughing and expectoration; often bronchitis, and 20 following the swallowing of a foreign body. Ten of these cases, illustrating special points, are described in detail and illustrated with roentgenograms.

It is important to follow up the cases with bronchography. A series of bronchograms gives valuable information in regard to prognosis and the advisability of surgical operation.—*Audrey G. Morgan.*

Moberg, Gunnar. Some views on the important part played by the pressure conditions in chest and abdomen for the radiographic examination of heart and lung. *Acta radiol.*, 1940, *21*, 1–20.

Ordinary routine roentgen examination of the chest often shows that the heart shadow changes in size from one examination to the next, though there is no apparent clinical reason for such a change. Sometimes the increase or decrease in the transverse diameter of the heart is as much as 1 or 2 cm., which is too much to be explained by the fact that one examination may have been made in systole and the other in diastole. The usual tendency in such cases is to look for some pathological change which is assumed to exist.

But from a discussion of findings in Valsalva's experiment, that is the making of an expiratory movement with the glottis closed and with the chest in a position of deep inspiration, it is evident that the variations in the size of the heart shadow, mentioned above, may be due to a Valsalva's experiment performed unconsciously by the patient during the examination. During such an expiratory movement there is increased pressure in the chest and also a rise of pressure in the abdominal cavity, re-

sulting in decreased size of the heart. The small asthmatic heart is probably caused by the hampered and prolonged expiration in asthma, which increases pressure in the thorax.

Attention is also called to the serious and sometimes fatal effects of raising intrathoracic pressure in patients with a diseased heart or high blood pressure. In one of the cases illustrated the patient had an acute attack of heart failure immediately after carrying out Valsalva's test. Such attacks and even death in patients with heart disease after straining at stool are not uncommon.

Illustrative roentgenograms are given.—*Audrey G. Morgan.*

Huizinga, E., and Behr, E. On the division of the lung segments. *Acta radiol.*, 1940, *21*, 314–325.

The authors investigated the modern division of the lung into segments on the basis of the examination of 125 left lungs. They found that the left upper lobe practically always consists of three segments: an apical segment, a lower anterior segment and a middle segment between them. The apical segment is generally the largest, the middle the smallest and the lower anterior one approximately midway between them in size. Among the 125 upper lobes examined 85 showed this picture. In the other 40 cases, too, the segment formation was typical but there was some variation in the ramification or bifurcation of the bronchi. The different methods of distribution of the bronchi are shown by diagrammatic drawings. In only 3 of the cases there was no middle segment.

The construction of the left lower lobe is more complicated. The upper dorsal segment is always found. The bronchus of this segment is a large dorsal branch which springs from the main bronchus before this ramifies into the other lower lobe bronchi. This segment occupies approximately half of the lower lobe. The rest of the lower lobe is divided into a medio-dorsal and a latero-ventral segment. These however vary in size and shape much more than do the segments of the upper lobe. Examples of these variations are described.

A series of roentgenograms of the lung after injection of lipiodol into the bronchial tree is given which show the various segments of the lung and the branches of the bronchi.—*Audrey G. Morgan.*

Fossati, Franco. Ernie, diverticoli ed essudati saccati del pericardio: sintomatologie e diagnosi differenziale radiologica. (Hernia, diverticula and sacculated exudates of the pericardium: symptomatology and differential roentgen diagnosis.) *Radiol. med.*, May, 1940, *27*, 343–365.

Hernias and diverticula of the heart were unknown for a long time and were definitely identified only by the study of Kienböck and Weiss in 1929. Only about 70 cases have been observed, many of these being chance findings on autopsy. Only 22 cases have been thoroughly studied roentgenologically and only 4 of these have been controlled by autopsy and one by operation.

Diverticula of the pericardium are circumscribed extroflexions of the pericardial sac, generally containing liquid and communicating with the pericardial sac through an opening of various sizes. True diverticula involve all the layers of the pericardium and are generally congenital. False diverticula are hernias of the serosa through a new-formed or more often preformed opening in the fibrous layer. The most frequent site is on the right external outline of the heart. They are generally round or oval or sometimes hour-glass shape with the larger pole downward. The clinical symptomatology is slight: a feeling of oppression, and pain points radiating to the shoulder or arm of the same side and sometimes a slight feeling of weakness, dyspnea on exertion, dry cough, anorexia, headache, slight fever, etc.

The roentgen picture is generally that of an opaque protrusion which cannot be dissociated from the cardiovascular shadow; the shape of the mass changes on respiration—it is elongated on inspiration. There are rhythmical lateral movements of the mass, which take place slightly later than ventricular systole. This picture is not absolutely pathognomonic, however, as it is sometimes seen in mediastinal dermoid cysts and other paracardiac masses. Hernia and diverticula cannot be differentiated roentgenologically. The cases will probably be found more numerous when sufficient attention is given to looking for them.

These conditions, however, can and must be differentiated from chronic sacculated exudate of the pericardium in which the enlargement of the pericardium is generalized and not localized as in hernia and diverticulum. While the symptomatology in the latter two conditions is slight

and consistent with long life and ability to work, in sacculated exudate it is sometimes severe and may even cause death. Moreover pericardotomy may give brilliant results in sacculated exudate but is absolutely useless in hernia or diverticulum.

Chimography is valuable in differentiating cyst and diverticulum from other mediastinal conditions such as aneurysm of the aorta. Roentgenograms and kymograms are reproduced and a discussion given of the differential diagnosis of these conditions from other pathological processes in the mediastinum, such as parietal aneurysm of the heart, enlarged right or left auricle, tumors of the pericardium, echinococcus cysts, aneurysm of the aorta or pulmonary artery, mediastinal tumors, and abscesses of the intrathoracic spinal column.—*Audrey G. Morgan.*

Pace, Lucio. Il quadro radiologico della ipertrofia timica nella seconda infanzia. (The roentgen picture of hypertrophy of the thymus in the second period of childhood.) *Radiol. med.*, May, 1940, *27*, 393–398.

Hypertrophy of the thymus is more frequent in the newborn and in early childhood than in the second period of childhood. It is a part of the exudative diathesis and is often accompanied by hyperplasia of the tonsils and lymph nodes. It is frequently accompanied by definite asthmatic symptoms, convulsions of the eclamptic type, eczematous eruptions or slight anemia.

It may, however, not be accompanied by any definite symptoms and is then shown only by roentgen examination. The author examined 300 children from three to six years of age in an institution for the prevention and cure of tuberculosis; 27 per cent of the children had a tuberculous heredity, 18 per cent a positive Pirquet reaction and 13 per cent roentgen signs of pulmonary tuberculosis. In this group he found only 6 children who showed roentgen signs of enlarged thymus, consisting of a triangular opaque shadow above the base of the heart shadow. The heart shadow was neither deformed nor enlarged. The triangular thymus shadow had its base upward, the upper boundary being at the sternoclavicular joint. Its opacity was homogeneous and the clear area representing the trachea could be seen passing through it. The lateral edges were very distinct and invaded the adjacent lung fields; the course was slightly convex outward. The outline of the hilum was normal. The lung fields were not changed. In some cases these shadows of the enlarged thymus may extend over the shadows of the great vessels and cover them and they may extend downward over the auricles, reaching to the ventricles.

The author gives some differential points between these shadows and others with which they might be confused, such as abnormal shadows of the great vessels, the shadows of mediastinal pleurisy and those of tracheobronchial adenopathy.

The percentage of enlarged thymus in his group of cases was small—2 per cent instead of the 5 per cent reported by Perkins. But Perkins examined children two years of age or less in whom enlarged thymus is more frequent. There were no clinical signs of enlarged thymus in these cases.—*Audrey G. Morgan.*

Stewart, Chester A. Tuberculosis. A follow-up study of children at Lymanhurst Health Center. *Am. J. Dis. Child.*, May, 1940, *59*, 1034–1049.

This paper is an analysis of the records of 10,003 children with an average age of nine years. Initial reactions to tuberculin were negative for 7,107 of these children and positive for the remaining 2,896. On entry to the clinic, roentgenograms of the chest were made of 84.3 per cent of the uninfected children and of 95.5 per cent of the infected patients. The percentage of children whose lungs were interpreted as normal on the basis of initial roentgenograms amounted to 92.9 for those with negative reactions to tuberculin and 57 for the tuberculin-sensitive group. Roentgenographically demonstrable lesions which were considered nontuberculous were revealed by 4.3 per cent of the roentgenograms of the children with negative reactions to tuberculin and by 4.7 per cent of the roentgenograms of the infected children. In each series of patients the incidence of lesions of this character tended in general to increase gradually in successive age groups. All of the remaining lesions reported by the roentgenologist for these two series of children were of the type which the tubercle bacillus produces.

Relatively benign pneumonic infiltrations deemed representative of the earliest roentgenographically demonstrable stage of the broad primary phase of the evolution of pulmonary tuberculosis were found in 166 members of the infected group. The incidence of such lesions

reached a maximum at about the third year of life and then diminished. Primary pneumonic tuberculous infiltrations were found only in the tuberculin-sensitive group. A general tendency for these lesions first to persist and later to resolve slowly was noted.

Calcified and fibrosed deposits were revealed by 2.8 per cent of the initial roentgenograms of the children with negative reactions to tuberculin. The incidence of these lesions tended to increase slightly with advancing age.

Calcified and fibrosed deposits were disclosed by 30.6 per cent of the initial roentgenograms of the infected children. For this series of patients the incidence of these lesions increased rapidly until the age of 8.5 years but subsequently manifested no consistent change. The calcified and fibrosed deposits were considered as representing an older stage in the evolution of primary pulmonary tuberculosis than was represented by the pneumonic tuberculous infiltrations found in 166 members of the series of infected patients.

Initial roentgen study of 2,767 tuberculous children disclosed 49 patients with chronic pulmonary tuberculosis of the adult type. This form of the disease made its first appearance at the seventh year of life and tended to increase in relative frequency in each sucessive age group.

Follow-up roentgenographic study: Follow-up roentgenographic examination extending throughout an average period of seven years of 2,670 children with negative reactions to tuberculin and of 1,784 tuberculin-sensitive children disclosed marked changes in roentgenographic findings chiefly for the infected group, in which the incidence of roentgenographically normal lungs decreased from 53.9 to 36.9 per cent.

During the follow-up roentgen study of the infected patients the incidence of primary pneumonic tuberculous infiltrations decreased from an average of 7.9 per cent to one of 0.7 per cent. This change resulted from the spontaneous resolution which these lesions were observed to undergo.

The incidence of calcified and fibrosed deposits changed from an initial 31.6 per cent to a final 53.1 per cent. A major portion of this change resulted from the appearance of lesions of this character in many of the infected children whose initial roentgenograms revealed no evidence of pathologic conditions.

During the course of the follow-up roentgen study the incidence of chronic pulmonary tuberculosis increased from 2.7 per cent to 6 per cent in the infected group.

During the course of the follow-up study serious forms of tuberculosis representative of the author's second clinically demonstrable phase of the evolution of the disease (chronic pulmonary miliary disease, tuberculous meningitis and osteoarticular tuberculosis combined) were acquired by 19 members of the originally uninfected group and by 98 members of the infected group.

The combined incidence of these four serious varieties of tuberculosis per thousand patients and per thousand person years of follow-up experience observed for the infected group was approximately tenfold that recorded for the children who entered the Lymanhurst Health Center with negative tuberculin reactions.

Stewart concludes:

1. The complex immunologic changes which infections with virulent tubercle bacilli produce do not provide a solution of the problem of human tuberculosis.

2. Infections with this organism serve to perpetuate tuberculosis in successive generations of man.

3. The eradication of tuberculosis is contingent on the prevention of infections with virulent tubercle bacilli.—*R. S. Bromer.*

ABDOMEN

Skarby, Hans G. Freies Gas in der Bauchhöhle als Zeichen von Perforation. (Free gas in the abdominal cavity as a sign of perforation.) *Acta radiol.*, 1940, *21*, 263–273.

The author discusses the cases examined for free gas in the abdomen at the University Hospital in Upsala from 1920 to 1939. The total number of cases examined was 261 and in 118 of them there was free gas in the abdominal cavity.

The best method of demonstrating free gas in the abdomen is to have the patient lie on his right or left side or back and direct the rays horizontally over the highest part of the abdomen, that is the right or left flank or, if the patient is on his back, the front of the abdomen. Most of the cases in which free gas was found were ones of perforated ulcer of the stomach or duodenum; gas was demonstrated in 69 of 107 of these cases. Other conditions in which free gas was found were perforating cancer of the stomach, perforating cancer, ulcer or diver-

ticulitis of the colon, ulcer of the small intestine, perforating abdominal injuries, subcutaneous rupture of the intestine, perforated appendicitis, subphrenic abscesses and other gas abscesses. Among other cases in which examination was made on suspicion of gas but no perforation was found were ones of acute disease of the bile tract, appendicitis, hysteria, gastritis, cancer of the stomach, pancreatitis, nonperforated ulcer of the stomach or duodenum, peritonitis, including the tuberculous form, contusions of the abdomen, stone of the kidney or ureter, ileus, colitis, lymphoma, mediastinitis, uremia (a total of 72 cases).

The material shows the increasing mortality and the increasing number of cases with positive roentgen findings as the time between the perforation and the examination increases. It also shows a considerable degree of parallelism between the size of the perforation and the probability of positive roentgen findings.—*Audrey G. Morgan.*

LICHT, ERIK DE FINE. Roentgen diagnosis of ileus. *Acta radiol.*, 1940, *21*, 32–38.

The author, who is the chief radiologist of the Gentofte County Hospital in Denmark, has found 142 cases in four years in which the roentgen findings resembled those of ileus. In examining for ileus he tried to obtain motionless roentgenograms and therefore made the exposures as brief as possible. He always used a Potter-Bucky diaphragm and examined by preference with the patient standing; if this was not advisable the patient was examined lying on his back and fluid levels were then demonstrated by lateral examinations. If necessary, the patient was placed on one side for examination for accumulations of gas in the peritoneum.

The cases are divided into those of verified mechanical ileus of the small intestine, 33; cases of ileus cured by means of prostigmin, 50; verified mechanical ileus of the colon, 25; verified paralytic ileus, 22; among the other 12 cases with roentgen findings of ileus there was one in which distended intestinal loops and fluid level were demonstrated and operation showed thrombosis of the mesentery; another case of gastric and duodenal ileus was caused by tumor of the pancreas.

The finding of a fluid level on roentgen examination for ileus is of great importance. The diagnosis is almost certain if this is accompanied by gaseous distention of the intestine. Gas distention alone does not justify the diagnosis of ileus. Repeated examinations are valuable for showing changes in the severity of the picture. It is not possible to differentiate between mechanical and paralytic ileus by roentgen examination alone. In cases of ileus of the colon this question can often be settled by giving an opaque enema.

Roentgen pictures resembling those of ileus are frequently seen after operation and after abdominal trauma similar pictures are seen. In true ileus the absence of a fluid level is rare and if there is neither a fluid level nor an abnormal accumulation of gas ileus is highly improbable. —*Audrey G. Morgan.*

FUGAZZOLA, FRANCO. Distonie duodenali e malattie del tubo digerente. (Duodenal dystonia and diseases of the digestive tract.) *Radiol. med.*, May, 1940, *27*, 366–381.

Thirteen cases are discussed and illustrated with roentgenograms in which dystonic conditions of the duodenum were associated with various diseases of the digestive tract. Some authors have held that such conditions of the duodenum are brought about only by reflexes from the diseased appendix but the author found them also in diseases of the right colon and gallbladder. In some cases there was spasm of the duodenum and in others atony. In atony the roentgen picture was like that seen in ulcer and tumor of the stomach. Generally the bulb was asymmetrical and only partially filled with contrast medium. In some cases its shape was preserved but it was larger than normal. Sometimes the bulb was round. Prolonged observation is required to demonstrate atony of the duodenum. Change of tonus of the duodenum is shown by anomalies in peristalsis and changes in caliber, shape and mucous membrane relief.

These cases of dystonia of the duodenum may be caused by appendicitis, periduodenitis, adenopathy or mesenteritis. In some of the author's cases adhesive bands could be seen as the cause. But in some cases there were no demonstrable anatomical changes which could have affected the duodenum. In these cases the change in the duodenum must be a reflex phenomenon brought about by stimulation of the celiac plexus. The author believes there is always some organic irritation which causes these conditions of dystonia and that therefore when

such an anomaly of the duodenum is seen a careful search should be made for its cause in some lesion of the digestive tract or abdominal glands.—*Audrey G. Morgan.*

Fabiani, Fabio. Scomparsa dell'immagine radiological di "nicchia" e guarigione anatomica di ulcera della piccola curva gastrica. (Disappearance of the roentgen picture of niche and anatomical healing of an ulcer of the lesser curvature of the stomach.) *Radiol. med.*, May, 1940, *27*, 398–402.

There is still considerable difference of opinion as to whether the disappearance of a niche in the roentgenogram means cure of the ulcer. The author describes a case as a contribution to the settlement of this question.

A man of forty-two entered the hospital with the typical symptoms of gastric ulcer. Roentgen examination showed a niche in the middle of the lesser curvature of the stomach the size of the end of the thumb. As the patient was in very poor general condition it was decided to give him preparatory medical treatment before operation. He was given 24 injections of histidin. During this treatment the symptoms of ulcer improved very greatly and a roentgen examination on the thirtieth day did not show any sign of niche.

The patient was operated on. There was no ulcer but at the junction of the middle and upper thirds there was a spot about the size of a penny where the serosa was slightly thickened and umbilicated, but smooth and shining. The stomach wall here was a little more rigid than normal. A subtotal resection was performed and the stomach and intestine united by a Reichel-Polya operation. The patient was discharged cured.

Histological examination of the specimen showed a gastric ulcer in an advanced stage of repair. A detailed description of the histological findings is given and the photomicrographs and roentgenograms are reproduced. This is one of a series of similar cases of which a more detailed study is being made.—*Audrey G. Morgan.*

Casati, Annibale. Studi sull'immagine radiologica della mucosa gastro-intestinale. (a) Stomaco normale. (Study of the roentgen image of the gastrointestinal mucosa. (a) Normal stomach.) *Radiol. med.*, June, 1940, *27*, 425–439.

The author describes his special technique for examining the stomach mucosa. He uses a distance of 70 cm., an exposure time of two to three tenths of a second, Potter-Bucky diaphragm and reinforcing screen; tube with a rotating anticathode (Rotalix), with a focus 1.2 × 1.2 mm., with a high intensity of current and an S.D. Metalix apparatus with four valves. The tube with a rotating anode bears much higher charges than one with a fixed anode. With this method the details are very clear and the contrast striking.

He uses a pure barium sulphate prepared by a special physicochemical method in the presence of a catalyzing agent that makes it perfectly colloidal. This aqueous solution does not precipitate until after so long a time that the precipitation is negligible practically. This solution is superior for his purpose to the creamy solution used by many workers in which gum tragacanth is used to homogenize the preparation.

He uses only a very small amount of the solution—between 20 and 40 cc. One of the difficult points in the technique is to determine the amount to be used in each individual case, for the capacity of the stomach and the extent of the mucosa differ in different cases, not only because of actual differences in size but also from differences in tonus. When just the right amount is used a very thin layer of barium is spread over the whole mucous membrane. This shows not only the longitudinal sulci which appear in the ordinary examination, but also the delicate transverse sulci giving a network with polygonal meshes, particularly clear along the greater curvature. There is also a design of little circles representing, he thinks, the gastric areolae. This method gives a clearer and more detailed picture of the stomach mucosa than has heretofore been obtained by any other method.—*Audrey G. Morgan.*

Baccaglini, Mario. Grossi diverticoli duodenali. (Large duodenal diverticula.) *Radiol. med.*, June, 1940, *27*, 492–493.

A woman of fifty-seven had for about two years had a feeling of indefinite discomfort in the epigastrium, particularly at night. If she took much liquid she vomited. Rarely she had a burning sensation in the stomach. A month before coming for examination she had intense pain in the upper part of the abdomen radiating to the back. This continued for eight days and then gradually stopped as a result of

taking intestinal disinfectants. Following a second attack of pain she came for examination. Physical examination did not show anything except slight anemia and slight pain on pressure over McBurney's point.

Roentgen examination of the digestive tract showed two gas and liquid levels laterally from the upper lumbar vertebrae. An esophageal sound entered a diverticulum in the first portion of the duodenum which on filling with contrast medium was found to correspond to the right gas-liquid level; another diverticulum of about the same size and the same characteristics was seen at Treitz' angle. It corresponded to the gas-liquid level seen to the left of the spinal column and made an imprint on the lesser curvature and posterior wall of the stomach when the patient was lying down.

Diverticula of the duodenum were not diagnosed in the living subject until after the introduction of roentgenography. Now they are of clinical as well as anatomical interest. They are generally in the second portion of the duodenum, especially near Vater's papilla. Their pathogenesis is not known.

They may remain latent throughout life or cause dyspeptic symptoms, or symptoms of ulcer or stenosis of the pylorus or disease of the liver or pancreas. These symptoms are probably due to stagnation of their contents or to inflammation in or around them.

The characteristic roentgen sign is the appearance of a round opaque shadow near the duodenum. Sometimes the opening between the duodenum and the diverticulum can be seen. The appearance of two gas-liquid levels beside the spinal column, as seen in the above case, is quite exceptional and could be caused only by stagnation of contents and accumulation of gas in quite large diverticula. Mobility and pain on pressure may indicate diverticulitis or peridiverticulitis.

The interest in this case lies in the rarity of such structures in the first portion of the duodenum and the unusually large size of the diverticula.—*Audrey G. Morgan.*

BORIANI, GIUSEPPE. Anatomo-radiografia dell'-ulcera gastrica. (Roentgenography of anatomical specimens of ulcer of the stomach.) *Radiol. med.*, June, 1940, *27*, 474–480.

The author made roentgen examinations of the specimens resected in 13 operations for ulcer of the stomach. The cases are described briefly and the roentgenograms are reproduced. He filled the resected specimens with barium solution and made roentgenograms which showed the following results: (1) the niche is almost always on the lesser curvature; (2) the niche is almost always buried in a sort of medallion of inflamed tissue to which the author gives the name of the bed of the niche; (3) convergence of folds toward the niche is perhaps not as common as is usually believed; (4) this convergence is in part at least a result of a process of repair as it apparently follows the absorption of the bed of the niche.—*Audrey G. Morgan.*

CAPUA, ANTONIO. Diverticolosi del tenue. (Diverticulosis of the small intestine.) *Radiol. med.*, May, 1940, *27*, 412–413.

A patient thirty-five years of age was sent for roentgen examination for actinomycosis. On the anterior wall of the thorax just below the submammary sulcus on the left side there was a swelling the size of a pigeon's egg in the skin and subcutaneous tissue. It was bluish-brown, fluctuating in the center and a purulent substance was being discharged through a small opening. Another infiltration of the skin and subcutaneous tissue was seen around the umbilicus. Here there was a large operation scar that had fistulized. Microscopic examination of the discharge showed typical actinomycosis which had been very resistant to iodine treatment and therefore the surgeon had operated to remove the periumbilical infiltration. It had recurred, however, at its former site and also at the submammary site mentioned above. The patient was then sent for roentgen treatment but, as there were fistulas in the umbilical region, before giving the treatment a roentgen examination of the digestive tract was made to exclude possible involvement of the abdominal cavity and intestines.

The examination did not show any lesions of the digestive tract, but in the second portion of the duodenum there was a typical diverticulum. There were other small diverticula in the first loops of the small intestine. These diverticula were the size of a millet seed to that of a hazelnut. At the sixth hour, when the patient was examined again for the purpose of observing the colon and appendix, the small intestine was completely empty and there was no retention of contrast medium in either the duodenal diverticulum or those in the small intestine.—*Audrey G. Morgan.*

Luccioni, Consuelo. Ematoma encistato della milza studiato radiologicamente con l'ossido di torio. (Encysted hematoma of the spleen studied roentgenologically with thorium oxide. *Radiol. med.*, June, 1940, *27*, 466–471.

A case is described in a man of fifty-three who was struck a hard blow in the left flank. A physician who examined him did not find any injury of the abdominal organs. But as severe pain persisted in the left half of the thorax after some days the patient called in another physician who also found nothing abnormal. But after about ten days, called in again, he found a slight pleural effusion on the left side. Under treatment for this the patient improved, but suddenly, after about three weeks, he again had intense pain in the flank, accompanied by dyspnea, temperature of 38° C. and enlargement of the abdomen. Two physicians found enlargement of the spleen; liver normal, no free effusion in the peritoneum.

The author examined the spleen, giving three injections of thoriofanin at intervals of two days; altogether 75 cc. was injected without any disturbance of any kind. This showed an enlarged shadow in the splenic region with no contraction of the spleen; there was no abnormality in the blood count and no interference with the function of the reticulo-endothelial system. The uniform coloring with thorium proved that the collection of fluid around the spleen was not abscess, infarct or parasitic cyst. The only possible remaining diagnosis was encysted hematoma of the spleen.

Splenectomy was advised and refused. As the patient felt relatively well he did not want to submit to so serious an operation. About a year later, as was to be expected, on a sudden effort the spleen ruptured and of course the patient died.

The author does not know of any other such case that has been diagnosed by the use of thorium.—*Audrey G. Morgan.*

Kretschmer, H. L. Retroperitoneal lipo-fibrosarcoma in a child. *J. Urol.*, Jan., 1940, *43*, 61–74.

A lipofibrosarcoma is usually found during the fourth to fifth decade; its presence in a child is rare. The author could find no such tumor in a child reported in the literature. He reports a case occurring in a two year old female child. The patient was brought to the hospital for an abdominal tumor. Physical examination revealed a hard smooth mass extending from the right costal arch to the iliac fossa and to the border of the right rectus muscle. A survey roentgenogram of the abdomen showed a large oval shadow with a dense sharply defined border and a mottled center. The shadow extended from the lower border of the liver to the iliac crest and to the vertebral column in the midline. The roentgenologist suggested the presence of a lipoid-containing cyst. A pyelogram showed mesial displacement of the right renal pelvis as well as upward displacement. This kidney also appeared to be rotated. A diagnosis of retroperitoneal tumor was made. No change was perceptible after four deep roentgen therapy treatments, dose not specified. At operation a retroperitoneal tumor was found which was not attached to the kidney. Histologic examination showed lipofibrosarcoma. Nine deep therapy treatments were given postoperatively. There was no sign of recurrence two years later.

The author summarizes 6 cases of retroperitoneal lipoma reported in the literature as occurring in children. The theories as to etiology are discussed. They are inconclusive. Growths that are histologically benign are prone to recur. The author suggests that these tumors actually have malignant areas if careful search is made. Possible points of origin are the lumbar, perirenal and prevertebral fat, fat along the promontories of the sacrum, and fat in the true pelvis. Secondary pressure effects on the kidney and ureter may lead to hydronephrosis or pressure atrophy. The commonest symptoms are abdominal tumor and pressure symptoms from the digestive or urinary tracts.

Radical extirpation is the only treatment. Preoperative irradiation should be employed with large tumors and postoperative irradiation where malignant changes are demonstrated.—*R. M. Harvey.*

Tiffin, Mary E., Chandler, Loren R., and Faber, Harold K. Localized absence of the ganglion cells of the myenteric plexus in congenital megacolon. *Am. J. Dis. Child.*, May, 1940, *59*, 1071–1082.

A case is reported of megacolon in which the sigmoid flexure was of normal caliber and the entire colon above that segment was enormously dilated and hypertrophied. The production of spinal anesthesia and the administration of mecholyl and prostigmine caused contraction of the bowel without propulsion of its

contents. Sympathectomy did not influence the condition favorably. Syntropan had no definite effect.

The cells of Auerbach's plexus were normal in number and appearance throughout the hypertrophied and dilated portion of the bowel but were greatly diminished or absent in the undilated sigmoid colon.

The authors believe that this case and others similarly studied indicate that a subgroup of Hirschsprung's disease exists in which localized absence of the peripheral neurons of the parasympathetic system causes a functional partial obstruction in the same region, with secondary dilatation and hypertrophy in the bowel cephalad to it. They regard it as uncertain what proportion of cases of Hirschsprung's disease belongs in this category. The condition described appears to be closely related to that existing in cardiospasm with megaesophagus.—*R. S. Bromer.*

Law, John L. Treatment of megacolon with acetylbetamethylcholine bromide. *Am. J. Dis. Child.*, August, 1940, *60*, 262–282.

In this paper, Law presents in detail, with 15 illustrative cases, a successful management of megacolon with acetylbetamethylcholine. In his summary, he states that experimental evidence, neurosurgical interruption of the sympathetic nerves to the colon and cholinergic drug action, support the neurogenic theory of megacolon as a functional imbalance of the autonomic nervous system supplying the colon. Detailed theories of the exact pathologic mechanism because of incomplete, imperfect and conflicting anatomic evidence are not yet justified. One of two basic etiologic working hypotheses is probable: (*a*) hyperactivity of the sympathetic nerves to the colon and (*b*) diminished tonus of the parasympathetic innervation of the colon with associated insufficient relaxation of the internal sphincter.

Decision for sympathectomy, the remedial agent for hyperactivity of the sympathetic nerves, is usually empiric, as there is no exact test for sympathetic hyperactivity. Sympathectomy is generally not indicated in the very young, and results are minimal in those patients with great colonic dilatation and weak musculature. Patients with colonic hypertrophy and vigorous visible peristalsis respond best to operation.

Administration of a cholinergic drug, the remedial agent for diminished tonus of the parasympathetic nerves, is empiric and the only known functional test of tonus.

Law reviews the pharmacologic action of acetylcholine and its derivatives. Their toxic actions and the instability of some of the early products explain the general defection from a drug physiologically potent in treatment of megacolon. Acetylbetamethylcholine (hydrochloride or bromide) has not been therapeutically successful in the past because the time element in rectifying autonomic imbalance has not been duly considered.

When a diagnosis of megacolon is made, the relief of the obstinate constipation is obtained by using each day or every other day enemas of oil or soapsuds and by giving liquid petrolatum orally each night in quantities of one-half to one ounce. After the colon has been unloaded, a sigmoidoscopic examination may be indicated, followed by an enema of barium sulfate for fluoroscopic or topical roentgen diagnosis. Excessive and damaging colonic distention and constipation secondary to a barium enema can frequently be avoided by instilling a thin mixture of barium sulfate (one-half strength) in moderate quantity under fluoroscopic control. The colon may have to be evacuated with enemas, liquid petrolatum and acetylbetamethylcholine bromide. The administration of this drug is then begun as a remedial agent in moderate daily doses, gradually increased to a point of effectiveness, short of disturbing toxicity, assisted with liquid petrolatum daily and enemas when required.

Law's experience has shown that optimal times for administration are one-half to one hour after breakfast, in midafternoon or at any juncture to parallel and enhance an observed daily intestinal rhythm. If given before breakfast, nausea, abdominal pain, vomiting and other toxic symptoms are common. A margin of five to ten days is allowed and expected in order to right an autonomic imbalance and to set up acquired reflexes which are constantly at work regulating intestinal function. An average initial dose of acetylbetamethylcholine bromide is 0.1 gm. increased, if necessary, in two or three days to 0.2 gm. and after several days, if indicated, further increased with the addition of 0.1 to 0.2 gm. administered in midafternoon. Usually 0.2 gm. after breakfast is effective without the addition of the dose in the afternoon.

As the drug becomes effective enemas are discontinued, though the use of liquid petrolatum is continued as a mild mechanical aid. At times 0.2 gm. morning and afternoon is required to initiate movements. This quantity may cause diarrhea, in which case it is accordingly reduced. When stabilized to a dosage which produces one to two stools daily, the patient is discharged, usually with instructions to take 0.2 gm. each morning one-half hour after breakfast, 1 to 2 tablespoonsful of liquid petrolatum each evening and an occasional enema in the event of constipation or distention.—*R. S. Bromer.*

GENITOURINARY SYSTEM

Smith, E., and Orkin, L. The renal digestive reflex. *J. Urol.*, Jan., 1940, *43*, 1–19.

The growing literature testifies to the recognition of the association of digestive tract symptoms with upper urinary tract disease. The authors review the literature in which gastrointestinal symptoms have occurred as a result of nephroptosis, urinary calculi, hydronephrosis, ruptured renal pelvis and many other primary renal conditions. Their own study was limited to surgical renal lesions with normal kidney functions, with no acute inflammatory process and in which the symptoms and signs had led to a diagnosis of primary gastrointestinal disease. In a series of 487 cases, 50 patients were found in whom the history and physical findings indicated a digestive tract lesion but in whom a urological study showed an upper urinary tract lesion to be the cause of the symptoms. Twelve cases under the general heading of dyspepsia were originally diagnosed gastric and duodenal ulcer, carcinoma, pylorospasm, hyperacidity and gastric neurosis. Twenty-three cases had been diagnosed either acute or chronic appendicitis. Ten cases were diagnosed acute or chronic cholecystitis and cholelithiasis. Five cases were diagnosed intestinal obstruction.

It is interesting to note the number of cases in which the true nature of the actual urinary tract cause for the intestinal symptoms was suggested by means of the roentgenogram. In 20 per cent of cases the actual cause was indicated by the flat film or intravenous urography and in another 36 per cent by negative gastrointestinal roentgenograms. The most frequent true final urological diagnoses were ureteral calculus, hydronephrosis and hydroureter and nephroptosis. In the majority of cases right renal lesions gave symptoms referred to the stomach, biliary system or appendix, and left-sided renal lesions gave symptoms referred to the large bowel.

The authors explain the mechanism of the renal digestive reflex on the basis of common innervation. The kidney receives its nerve supply from the renal plexus, the majority of whose fibers are contributed by the celiac ganglion. Through this ganglion the renal plexus communicates with the greater splanchnic nerve. It also communicates with the fibers from the sixth thoracic to the first lumbar segments by way of the splanchnic nerves. The visceral nerves of the kidney originating in the tenth thoracic to the second lumbar segments have reflex communications with these segments. Thus we get cutaneous hyperesthesia through the somatic branches of these segments and also reflexes referred to the visceral branches supplying the gallbladder and intestinal tract. Impulses from the kidney to the spinal cord may pass upwards in the tractus solitarius to the vagus nucleus and connect there with parasympathetic fibers to the upper intestinal tract. —*R. M. Harvey.*

Hareide, Ingvard. Über die Röntgenuntersuchung bei Nierenverletzungen unter besonderer Berücksichtigung der intravenösen Urographie. (Roentgen examination in injuries of the kidney, with special reference to intravenous urography.) *Acta radiol.*, 1940, *21*, 292–313.

Urographic examination is of great value in kidney injuries because it shows more clearly than clinical examination the nature and severity of the anatomical changes which are the decisive factors in determining treatment. If the kidney pelvis is injured, it is important to demonstrate this fact as early as possible while the conditions for operation are still favorable. Even if the kidney is so severely injured that nephrectomy is clearly indicated it is important to know the condition of the other kidney, which may furnish a contraindication to operation.

Intravenous pyelography is to be preferred to the retrograde method and the author has used this method exclusively. He discusses the results in cases from the literature and in 16 cases of his own, histories of which are given.

The ordinary roentgenogram usually shows

perirenal hematoma. If the rupture is subcapsular and there is no hemorrhage around the kidney the organ is enlarged. The most constant urographic finding in injury of the kidney is deformity of the kidney pelves or defects in their filling. If there is a tear in the wall of the pelvis it causes the characteristic sign of contrast outside the pelvis.

Kidney function in injuries of the kidney may be normal, decreased or entirely abolished. Kidney function in trauma seems to be dependent on three factors: the condition of the kidney parenchyma, that of the circulation and the permeability of the ureter. Even in very slight injury there may be a clot in the ureter which interferes with discharge of the urine.

The objection has been urged against intravenous pyelography that the image is not as rich in contrast as that of the retrograde pyelogram. This is true, but there is generally sufficient contrast to show the anatomical changes. The possibility of localizing the tear in the kidney pelvis is one of the great advantages of pyelography. If there is a copious retroperitoneal hemorrhage the decision as to whether operation must be performed at once or whether it is safe to delay it and make another pyelographic examination must be based on the clinical symptoms.—*Audrey G. Morgan.*

OPPENHEIMER, G. D. Evaluation of roentgenography of surgically exposed kidney in treatment of renal calculi. *J. Urol.*, Feb., 1940, *43*, 253–264.

The incidence of recurrence after conservative operation for renal calculi has been variously reported from 4.6 to 60 per cent. The incidence would be reduced greatly if the problem of "left-over" or residual recurrence were solved. Several authors have advocated kidney roentgenographic control at operation to find stones or stone fragments which cannot be palpated. The author's technique is to remove all the stones that can be located, raise the kidney by a gauze sling, place a Bucky kidney film in a thin sterile rubber bag against the posterior aspect of the kidney; needles are inserted into the convex border of the kidney as markers and then a 3 second exposure at 36 inch distance is made with a shock proof bedside unit. The films are then developed in an adjacent emergency darkroom and further removal attempted if indicated. The author feels this method is more accurate than the roentgenoscopic. By using this procedure it was possible to remove residual calculi from 15 of 33 patients in which the fragments could not be palpated. With an additional series of 52 patients 34 per cent had stone fragments removed which were only revealed by the above procedure.

The author has encountered cases in which additional stones were hidden behind large stones, whole stones were actually many small stones, and also frequent changes in position of stones even when films were exposed the day of operation. The disadvantages of the system are prolonged operating time, the presence of a technician in the operating room for the required time, the fact that visible stones may not be removable, non-opaque calculi, and the presence of calcified shadows which are not calculi.—*R. M. Harvey.*

MINTZ, E. R. Pedunculated neurofibroma of the bladder. *J. Urol.*, Feb., 1940, *43*, 268–274.

Neurofibroma of the bladder is rare and when it does occur is usually associated with multiple neurofibromatosis. This disease consists of multiple fibrous nodules in the subcutaneous tissue along the course of cutaneous nerves. Sarcomatous degeneration has been reported. The author reports a case of bladder neurofibroma, not associated with general neurofibromatosis. The tumor weighed 315 grams and was the largest of its type reported. The patient was a white male, aged twenty-eight, who complained of hematuria of five years' duration, right flank pain and tenderness of four months' duration. Physical examination revealed a nontender suprapubic mass 6 cm. in diameter. A flat abdominal film showed multiple areas of calcification in the lateral portions of the pelvis on each side. A tuberculous origin was suspected. Intravenous urography showed a slight dilatation of the left ureter and renal pelvis and a marked dilatation on the right side. A cystogram showed a lobulated mass 11 cm. in diameter completely filling the bladder. The calcifications reported on the flat film were seen to lie in the tumor. Cystography confirmed the presence of a large bladder tumor.

Pathologic examination after operative removal of a large pedunculated tumor revealed a neurofibroma. No evidence of other cutaneous or visceral neurofibroma could be found.—*R. M. Harvey.*

Burford, E. H. Fibrous cavernositis. *J. Urol.*, Jan., 1940, *43*, 208–213.

Fibrous cavernositis is defined as a benign tumor of fibrous origin arising in the sheath of the corpora cavernosa of the penis. It was first described by La Peyronie in France in 1743. The author has collected over 600 cases in the literature. The disease usually occurs after middle life. The etiology is still unknown.

The tumor is attached to the fibrous sheath of the corpora cavernosa but never to the skin. The tumor is rather hard firm fibrous tissue usually occurring on the dorsum of the penis. The fibrous tissue of the growth is similar to fibrous tissue found elsewhere in the body and resembles keloids. The onset is slow and insidious. Pain on erection or incompatability at intercourse are the common presenting symptoms. Urinary difficulties are uncommon. The differential diagnosis should include trauma, gonorrhea, syphilis and tumors. Prognosis should be guarded but is usually good. Many forms of treatment have been suggested. The best results have been obtained with radium or roentgen rays or some combination of the two. The author has used the radium plaque almost exclusively. He states that skin irritation or even a burn should be expected with this form of treatment. He uses one to three needles of radium element (strength not stated), filtered by 1 mm. of lead, placed parallel to one another one-quarter inch apart, and the whole screened by 1 mm. of rubber. His exposures vary from 67.5 to 300 mg-hr., with the average being 150 mg-hr. Usually only one exposure was given, occasionally two. He reports 39 per cent cures, 45 per cent improvements, and 16 per cent failures with this technique. This record is much better than the usual reported results in this condition.—*R. M. Harvey.*

Graves, R. C., and Flo, S. Carcinoma of the scrotum. *J. Urol.*, Feb., 1940, *43*, 309–332.

Carcinoma of the scrotum was the first known occupational cancer. Its occurrence among those exposed to soot and oil led to the experimental production of animal tumors by means of tar and the search for carcinogenic agents among coal-tar products. The disease is rare and has a high virulence. At the Pondville Hospital the authors have seen 12 cases in twelve years. The ages varied from thirty-two to seventy-six, with the average being 52.7 years. In 9 of 14 cases there was a definite history of exposure to oil. The original lesion was usually described as a pimple or ulcer. There was no special predilection for any portion of the scrotum. Metastases occurred in the inguinal and femoral glands. In every instance the diagnosis was carcinoma or epidermoid carcinoma. The duration of life from the onset of disease until death averaged twenty-one months in 11 cases. Metastasis is by lymphatic embolism. A thorough description of the scrotal lymphatics is given by the authors.

In regard to treatment they feel that irradiation should not be relied upon for destruction of the tumor. They found the metastases to the groin to be particularly radioresistant. The thin scrotal wall is a poor field for radiation therapy due to lack of normal tissue defense. They advise electrosurgical removal of the growth-involved portion of the scrotum with a wide margin of normal tissue. They advise removal of the testicle and division of the spermatic cord well above the external ring at least on the side of the lesion. Radical and complete dissection of both groins must be carried out.—*R. M. Harvey.*

Jeck, H. S. Large solitary abscess of the kidney. *J. Urol.*, Jan., 1940, *43*, 28–34.

The author defines solitary abscess of the kidney as one lying wholly within the renal parenchyma and having no connection with the renal pelvis or perinephric space. He reports 2 cases. Intravenous urogram in the first case showed incomplete filling of the affected renal pelvis and fixation of the affected kidney. The edge of the psoas muscle shadow could be seen fairly distinctly on this side. In the second case the urogram showed marked compression of the affected renal pelvis. Pyelograms of the second case are shown before and after operation, the former showing marked compression of the kidney pelvis and the latter an apparently normal pelvis. *Staphylococcus aureus* is the common infecting organism. In many of the cases reported the patients gave a history of a preexisting boil or other staphylococcic skin infection, and it seems evident that the kidney infection is secondary. The diagnosis of solitary kidney abscess is suggested by a history of boils, carbuncles, osteomyelitis or other infection, chills, spiking temperature, loin pain, tenderness over the kidney, leukocytosis, ane-

mia and marked weight loss. The urinalysis is frequently negative. The pyelogram is of considerable aid. The chief signs are those of pressure, such as compression of the pelvis, unusual separation of the calyces, or displacement of a single calyx. In carbuncle of the kidney filling defects of the pelvis seem to be more common, and in many carbuncles no change is seen in the pyelogram. Also to be considered in differential diagnosis is perinephric abscess. In this condition the symptoms are less pronounced and the flat film usually shows scoliosis of the spine with the concavity toward the affected side, absence of the psoas muscle shadow on the affected side and fixation of the kidney.—*R. M. Harvey.*

MISCELLANEOUS

Gilardoni, Arturo. Il tubo Roentgen in scopia, grafia normale e grafia ultrabreve. (The roentgen tube in roentgenoscopy and in normal and ultrashort roentgenography.) *Radiol. med.*, May, 1940, *27*, 403–411.

The roentgen tube is the part of the roentgen apparatus that it most easily injured. In the great majority of cases it is injured or destroyed by an overcharge which heats it beyond the limits of its resistance. The author has made a study of the capacity of the roentgen tubes used for diagnostic purposes and discusses the causes which injure or destroy them.

With regard to the charge which can be borne without injury, the author distinguishes three types of use of these tubes: those with an exposure time of more than 30 seconds, used for reontgenoscopy; those with a time of 0.01 to 30 seconds, used for ordinary or normal roentgenography, and those with a time of less than 0.01 second used for ultrashort roentgenography. The third of these has practically not been studied at all.

The author himself, using the regmographic system of Cignolini, studied a generator or roentgen light with very brief exposure time, about a thousandth of a second or even less. From his experience he comes to the conclusion that, for very brief exposures, the charge may be quite strong without injuring the tubes. Graphs are given illustrating his findings.—*Audrey G. Morgan.*

Gilardoni, Arturo. Caratteristiche dell'apparecchio a condensatore per radiografia al millesimo di secondo e per regmografie. (Description of a condenser apparatus for roentgenography with an exposure time of a thousandth of a second and for regmography.) *Radiol. med.*, June, 1940, *27*, 481–489.

In a recent number of this journal the author described a generator of roentgen light to be used for an exposure time of a thousandth of a second or even less and for regmography. It was based on the principle of discharge by a condenser. In this article he studies the chief characteristics of this condenser apparatus. It is made up essentially of a high tension generator which charges a condenser. The electrical energy stored by the condenser is then discharged to the tube and in this way the roentgen exposure is made. A diagrammatic sketch of the apparatus is given. With this apparatus in normal subjects roentgenograms of the lungs can be made at a distance of 1.50 meters from focus to film, seriographies of the duodenum at 75 cm., and in general any roentgenograms of organs in movement in a thousandth of a second without injuring the tube.—*Audrey G. Morgan.*